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TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page for STN Seminar Schedule - N. America  
NEWS 2 AUG 15 CAOLD to be discontinued on December 31, 2008  
NEWS 3 OCT 07 EPFULL enhanced with full implementation of EPC2000  
NEWS 4 OCT 07 Multiple databases enhanced for more flexible patent  
number searching  
NEWS 5 OCT 22 Current-awareness alert (SDI) setup and editing  
enhanced  
NEWS 6 OCT 22 WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT  
Applications  
NEWS 7 OCT 24 CHEMLIST enhanced with intermediate list of  
pre-registered REACH substances  
NEWS 8 NOV 21 CAS patent coverage to include exemplified prophetic  
substances identified in English-, French-, German-,  
and Japanese-language basic patents from 2004-present  
NEWS 9 NOV 26 MARPAT enhanced with FSORT command  
NEWS 10 NOV 26 MEDLINE year-end processing temporarily halts  
availability of new fully-indexed citations  
NEWS 11 NOV 26 CHEMSAFE now available on STN Easy  
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searching  
NEWS 13 DEC 01 ChemPort single article sales feature unavailable  
  
NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.  
  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items  
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that  
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FILE 'HOME' ENTERED AT 15:40:27 ON 03 DEC 2008

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 15:40:32 ON 03 DEC 2008  
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STRUCTURE FILE UPDATES: 2 DEC 2008 HIGHEST RN 1078799-92-4  
DICTIONARY FILE UPDATES: 2 DEC 2008 HIGHEST RN 1078799-92-4

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

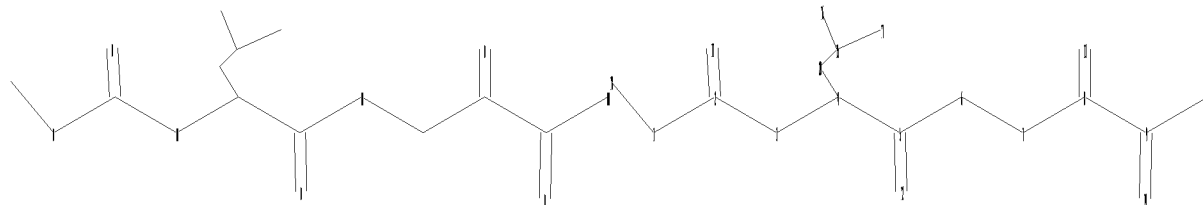
Please note that search-term pricing does apply when  
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on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10 582015 formula 1 open.str



chain nodes :  
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 20  
chain bonds :  
1-2 1-18 2-3 2-11 3-4 4-5 4-20 5-6 5-12 6-7 7-8 8-9 8-13 9-10 9-14  
15-17 15-16 15-20  
exact/norm bonds :  
1-2 1-18 2-3 2-11 3-4 5-6 5-12 6-7 8-13 9-10 9-14  
exact bonds :  
4-5 4-20 7-8 8-9 15-17 15-16 15-20

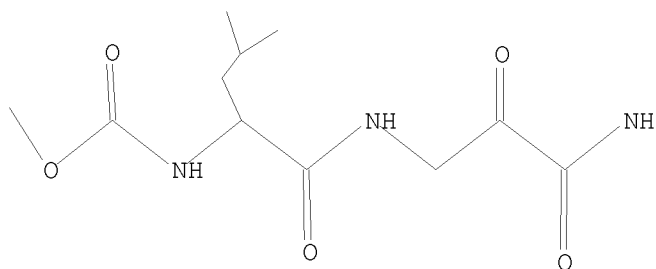
G1:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,Cy

Match level :  
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS  
18:CLASS 20:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS  
L1 STR



G1 H, Me, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu, Cy

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 sam
SAMPLE SEARCH INITIATED 15:40:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 260 TO ITERATE

100.0% PROCESSED      260 ITERATIONS      14 ANSWERS
SEARCH TIME: 00.00.01
```

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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:   4233 TO 6167
PROJECTED ANSWERS:      56 TO 504
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L2 14 SEA SSS SAM L1

```
=> s l1 full
FULL SEARCH INITIATED 15:40:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 5102 TO ITERATE

100.0% PROCESSED      5102 ITERATIONS      291 ANSWERS
SEARCH TIME: 00.00.01
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L3 291 SEA SSS FUL L1

```
=> fil caplus
COST IN U.S. DOLLARS      SINCE FILE      TOTAL
                           ENTRY      SESSION
FULL ESTIMATED COST      178.36      178.57
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FILE 'CAPLUS' ENTERED AT 15:40:57 ON 03 DEC 2008  
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FILE COVERS 1907 - 3 Dec 2008 VOL 149 ISS 23  
FILE LAST UPDATED: 2 Dec 2008 (20081202/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>  
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> s l3

L4 51 L3

=> d ti 1-51

- L4 ANSWER 1 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Molecular design to enhance the penetration into the retina via ocular instillation
- L4 ANSWER 2 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Cocrystal Structures of Primed Side-Extending  $\alpha$ -Ketoamide Inhibitors Reveal Novel Calpain-Inhibitor Aromatic Interactions
- L4 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Exploring Peptide-likeness of Active Molecules Using 2D Fingerprint Methods
- L4 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Contribution of calpains to photoreceptor cell death in N-methyl-N-nitrosourea-treated rats
- L4 ANSWER 5 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Retinal Penetration of Calpain Inhibitors in Rats After Oral Administration
- L4 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Imaging of neural and organ injury or damage
- L4 ANSWER 7 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Calpains as targets for inhibition of prion propagation
- L4 ANSWER 8 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Amelioration of retinal degeneration and proteolysis in acute ocular hypertensive rats by calpain inhibitor  
((1S)-1-(((1S)-1-benzyl-3-cyclopropylamino-2,3-dioxopropyl)amino)carbonyl)-3-methylbutyl)carbamic acid 5-methoxy-3-oxapentyl ester
- L4 ANSWER 9 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Preparation of aza-peptide epoxides as protease inhibitors
- L4 ANSWER 10 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Exploration of orally available calpain inhibitors. Dipeptidyl  $\alpha$ -ketoamide derivatives containing pyridine moiety
- L4 ANSWER 11 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Calpain Inhibition by  $\alpha$ -Ketoamide and Cyclic Hemiacetal Inhibitors Revealed by X-ray Crystallography

L4 ANSWER 12 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Protease inhibitor prodrug compounds and kits for treating muscle disorders and methods of use thereof

L4 ANSWER 13 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Preparation of leucyl  $\alpha$ -ketoamide derivatives as calpain inhibitors

L4 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Exploration of orally available calpain inhibitors: Peptidyl  $\alpha$ -ketoamides containing an amphiphile at P3 site

L4 ANSWER 15 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Development of  $\alpha$ -keto-based inhibitors of cruzain, a cysteine protease implicated in Chagas disease

L4 ANSWER 16 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Peptide ketoamide inhibitors for the treatment of neuropathies and hyperproliferative disorders

L4 ANSWER 17 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Design, Synthesis, Molecular Modeling Studies, and Calpain Inhibitory Activity of Novel  $\alpha$ -Ketoamides Incorporating Polar Residues at the P1'-Position

L4 ANSWER 18 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Preparation of diketohydrazine derivatives as cysteine protease inhibitors

L4 ANSWER 19 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Cellular Events Preceding Acetaminophen Cataractogenesis Studied by Confocal Fluorescence Microscopy

L4 ANSWER 20 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Epoxycarboxylic acid amides, azides and amino alcohols and processes for preparation of  $\alpha$ -keto amides by using them

L4 ANSWER 21 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Neuroprotectant formulations

L4 ANSWER 22 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Preparation of peptides and compositions containing them for treatment of parasitic infections

L4 ANSWER 23 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Peptidyl  $\alpha$ -keto amide inhibitor of calpain blocks excitotoxic damage without affecting signal transduction events

L4 ANSWER 24 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Epoxycarboxylic acid amides, azides and amino alcohols and processes for preparation of  $\alpha$ -keto amides by using them

L4 ANSWER 25 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Potent peptide  $\alpha$ -Ketohydroxamate inhibitors of recombinant human calpain I

L4 ANSWER 26 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Significance of Hydrogen Bonding at the S1' Subsite of Calpain I

L4 ANSWER 27 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
TI Preparation of tripeptide  $\alpha$ -ketoamides as serine and cysteine protease inhibitors

L4 ANSWER 28 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN

TI Calpain inhibition protects against virus-induced apoptotic myocardial injury  
  
 L4 ANSWER 29 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Synthesis and calpain inhibitory activity of  $\alpha$ -ketoamides with 2,3-methanoleucine stereoisomers at the P2 position  
  
 L4 ANSWER 30 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Efficacy of novel calpain inhibitors in preventing renal cell death  
  
 L4 ANSWER 31 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Passerini multicomponent reaction of protected  $\alpha$ -amino aldehydes as a tool for combinatorial synthesis of enzyme inhibitors  
  
 L4 ANSWER 32 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Preparation of hydroxamate-containing peptides as cysteine and serine protease inhibitors  
  
 L4 ANSWER 33 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Behavioral efficacy of posttraumatic calpain inhibition is not accompanied by reduced spectrin proteolysis, cortical lesion, or apoptosis  
  
 L4 ANSWER 34 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Preparation of peptide-containing  $\alpha$ -ketoamide cysteine and serine protease inhibitors  
  
 L4 ANSWER 35 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI The use of biologically active substances for influencing the extracellular space of sensory cells  
  
 L4 ANSWER 36 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Preparation of peptide  $\alpha$ -ketoamides as serine and cysteine protease inhibitors  
  
 L4 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI The use of calpain inhibitors to treat ocular neural pathology  
  
 L4 ANSWER 38 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI New inhibitors of calpain prevent degradation of cytoskeletal and myelin proteins in spinal cord in vitro  
  
 L4 ANSWER 39 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Preparation of peptidyl ketoamides as serine protease and cysteine protease inhibitors  
  
 L4 ANSWER 40 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Novel Peptidyl  $\alpha$ -Keto Amide Inhibitors of Calpains and Other Cysteine Proteases  
  
 L4 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Preparation of  $\alpha$ -ketoamide derivatives as cathepsin L inhibitors.  
  
 L4 ANSWER 42 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Peptidyl ketoamides as serine and cysteine protease inhibitors  
  
 L4 ANSWER 43 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Calpain inhibitor AK295 attenuates motor and cognitive deficits following experimental brain injury in the rat  
  
 L4 ANSWER 44 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors.

L4 ANSWER 45 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Calpain inhibitor AK295 protects neurons from focal brain ischemia: effects of postocclusion intra-arterial administration

L4 ANSWER 46 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI High-performance liquid chromatographic reversed-phase and normal-phase separation of diastereomeric  $\alpha$ -ketoamide calpain inhibitors

L4 ANSWER 47 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Stereospecific Synthesis of Peptidyl  $\alpha$ -Keto Amides as Inhibitors of Calpain

L4 ANSWER 48 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Use of calpain inhibitors in the inhibition and treatment of medical conditions associated with increased calpain activity

L4 ANSWER 49 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Peptide  $\alpha$ -keto ester,  $\alpha$ -keto amide, and  $\alpha$ -keto acid inhibitors of calpains and other cysteine proteases

L4 ANSWER 50 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Peptide keto amides, keto acids, and keto esters

L4 ANSWER 51 OF 51 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Use of calpain inhibitors in the inhibition and treatment of neurodegeneration

=> s US 20070004643 A1/pn  
 L5 1 US 20070004643 A1/PN

=> d ti

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Preparation of leucyl  $\alpha$ -ketoamide derivatives as calpain inhibitors

=> s l4 not patent/dt  
 L6 27 L4 NOT PATENT/DT

=> s l6 and pd<20041208  
 L7 17 L6 AND PD<20041208

=> d ti 1-17

L7 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Design, Synthesis, Molecular Modeling Studies, and Calpain Inhibitory Activity of Novel  $\alpha$ -Ketoamides Incorporating Polar Residues at the P1'-Position

L7 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Cellular Events Preceding Acetaminophen Cataractogenesis Studied by Confocal Fluorescence Microscopy

L7 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Peptidyl  $\alpha$ -keto amide inhibitor of calpain blocks excitotoxic damage without affecting signal transduction events

L7 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Potent peptide  $\alpha$ -Ketohydroxamate inhibitors of recombinant human calpain I

L7 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Significance of Hydrogen Bonding at the S1' Subsite of Calpain I

L7 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Calpain inhibition protects against virus-induced apoptotic myocardial injury

L7 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Synthesis and calpain inhibitory activity of  $\alpha$ -ketoamides with 2,3-methanoleucine stereoisomers at the P2 position

L7 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Efficacy of novel calpain inhibitors in preventing renal cell death

L7 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Passerini multicomponent reaction of protected  $\alpha$ -amino aldehydes as a tool for combinatorial synthesis of enzyme inhibitors

L7 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Behavioral efficacy of posttraumatic calpain inhibition is not accompanied by reduced spectrin proteolysis, cortical lesion, or apoptosis

L7 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI New inhibitors of calpain prevent degradation of cytoskeletal and myelin proteins in spinal cord in vitro

L7 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Novel Peptidyl  $\alpha$ -Keto Amide Inhibitors of Calpains and Other Cysteine Proteases

L7 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Calpain inhibitor AK295 attenuates motor and cognitive deficits following experimental brain injury in the rat

L7 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Calpain inhibitor AK295 protects neurons from focal brain ischemia: effects of postocclusion intra-arterial administration

L7 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI High-performance liquid chromatographic reversed-phase and normal-phase separation of diastereomeric  $\alpha$ -ketoamide calpain inhibitors

L7 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Stereospecific Synthesis of Peptidyl  $\alpha$ -Keto Amides as Inhibitors of Calpain

L7 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN  
 TI Peptide  $\alpha$ -keto ester,  $\alpha$ -keto amide, and  $\alpha$ -keto acid inhibitors of calpains and other cysteine proteases

=> d his

(FILE 'HOME' ENTERED AT 15:40:27 ON 03 DEC 2008)

FILE 'REGISTRY' ENTERED AT 15:40:32 ON 03 DEC 2008

L1 STRUCTURE UPLOADED

L2 14 S L1 SAM

L3 291 S L1 FULL

FILE 'CAPLUS' ENTERED AT 15:40:57 ON 03 DEC 2008

L4 51 S L3



L5 1 S US 20070004643 A1/PN  
L6 27 S L4 NOT PATENT/DT  
L7 17 S L6 AND PD<20041208

=> s 14 not 16  
L8 24 L4 NOT L6

=> s 18 and (pd<20041208 or ad<20041208 or prd<20041208)  
L9 22 L8 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)

=> s 17 or 19  
L10 39 L7 OR L9

=> d ibib abs hitstr l10

L10 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2006:769186 CAPLUS  
DOCUMENT NUMBER: 145:211345  
TITLE: Preparation of aza-peptide epoxides as protease  
inhibitors  
INVENTOR(S): Powers, James C.; Glass, Jonathan D.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 41pp., Cont.-in-part of U.S.  
Ser. No. 603,054.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

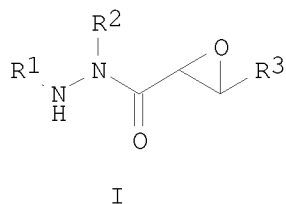
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060172952	A1	20060803	US 2006-338147	20060124 <--
US 20040048327	A1	20040311	US 2003-603054	20030624 <--
US 7056947	B2	20060606		
WO 2007087572	A2	20070802	WO 2007-US60991	20070124
WO 2007087572	A3	20071122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,  
KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,  
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,  
RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,  
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

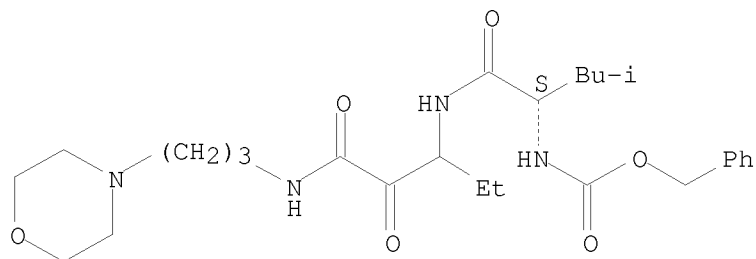
PRIORITY APPLN. INFO.:  
US 2002-394023P P 20020705 <--  
US 2002-394024P P 20020705 <--  
US 2002-394221P P 20020705 <--  
US 2003-603054 A2 20030624 <--  
US 2006-338147 A 20060124

OTHER SOURCE(S): MARPAT 145:211345  
GI



- AB The disclosure relates to aza-peptide epoxide I [R1 is M1, M2-AA1, M2-AA2-AA1, or M2-AA3-AA2-AA1, where M1 is NH<sub>2</sub>CO, NH<sub>2</sub>CS, NH<sub>2</sub>SO<sub>2</sub>, etc.; M2 is H or a group given for M1; AA1, AA2, and AA3 are side chain-blocked or unblocked amino acids with the L- or D-configuration or no chirality; R2 is (un)substituted alkyl, Ph, or naphthyl; R3 is (un)substituted (cyclo)alkyl, CO<sub>2</sub>H or esters, carboxamido groups, including amino acid derivs.] and their pharmaceutically-acceptable salts, which as caspase inhibitors can be used for the treatment and/or prevention of nerve degeneration in mammals. The compds. can be used in combination with calpain inhibitors to treat disease or pathol. conditions related to the activity of caspases and calpain associated with a specific disease or condition. Synthetic and biol. activity examples are provided. A bar graph shows a quant. measure of relative protection of calpain inhibitor AK295 [Cbz-Leu-Abu-CONH(CH<sub>2</sub>)<sub>3</sub>-4-morpholinyl (Cbz is benzyloxycarbonyl, Abu is  $\gamma$ -aminobutyric acid residue)], aza-peptide epoxide JG36 [Cbz-Asp-Glu-Val-AAsp-EP-CO<sub>2</sub>Et (AAsp is NHN(CH<sub>2</sub>CONH<sub>2</sub>)CO, EP is oxirane residue)], and a combination of AK295 and JG36 against vincristine-induced axonal degeneration at 6 days after treatment.
- IT 160399-35-9P, AK 295  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of aza-peptide epoxides as protease inhibitors)
- RN 160399-35-9 CAPLUS
- CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Currently available stereo shown.



- IT 150519-08-7 150519-09-8 150519-12-3  
 150519-18-9 150519-19-0 150519-20-3  
 150957-45-2 150957-46-3 150957-49-6  
 150957-50-9 207456-28-8 207456-33-5  
 207456-38-0 301295-26-1 301295-27-2  
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 677274-79-2 677274-80-5 677274-81-6  
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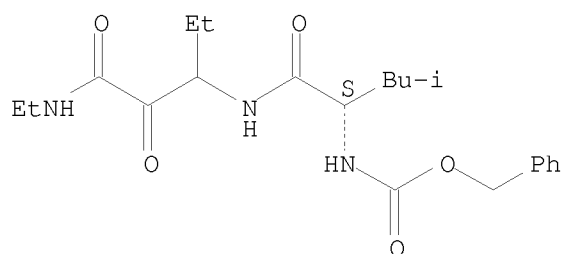
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 677274-98-5 677274-99-6 677275-00-2  
 677275-01-3 677275-02-4 677275-03-5  
 677275-04-6 677275-05-7 677275-06-8  
 677275-07-9 677275-08-0 677275-09-1  
 677275-10-4 677275-11-5 677275-12-6  
 677275-13-7 677275-14-8 677275-15-9  
 677275-16-0 677275-18-2 677275-19-3  
 677275-20-6 677275-21-7 677275-22-8  
 677275-23-9 677275-24-0 677275-25-1  
 677275-26-2 677275-27-3 677275-28-4  
 677275-29-5 677275-30-8 677275-31-9  
 677275-32-0 904299-60-1 904299-61-2  
 904299-62-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (preparation of aza-peptide epoxides as protease inhibitors)

RN 150519-08-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-(ethylamino)-2,3-  
 dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA  
 INDEX NAME)

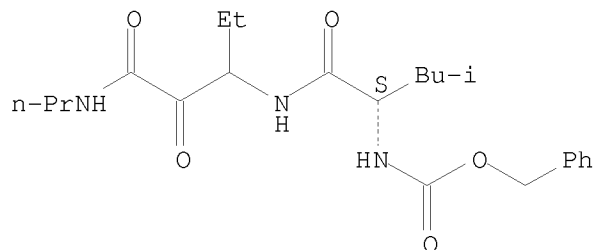
Absolute stereochemistry.



RN 150519-09-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-  
 (propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
 (9CI) (CA INDEX NAME)

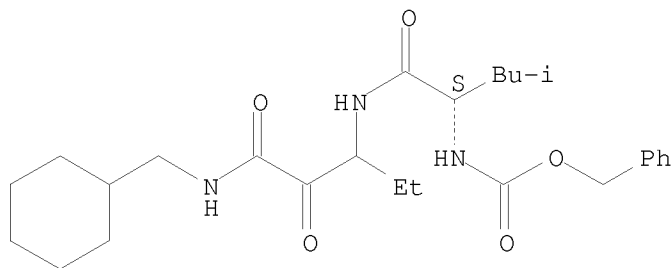
Absolute stereochemistry.



RN 150519-12-3 CAPLUS

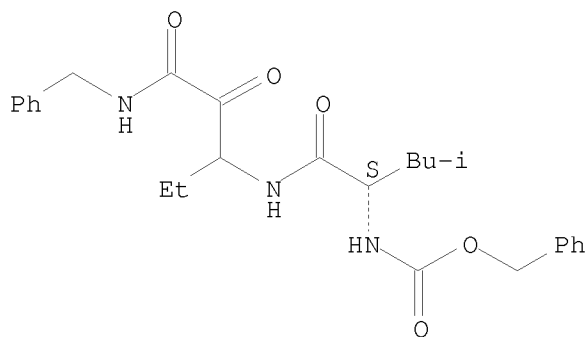
CN Carbamic acid, [(1S)-1-[[[3-[(cyclohexylmethyl)amino]-1-ethyl-2,3-  
 dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



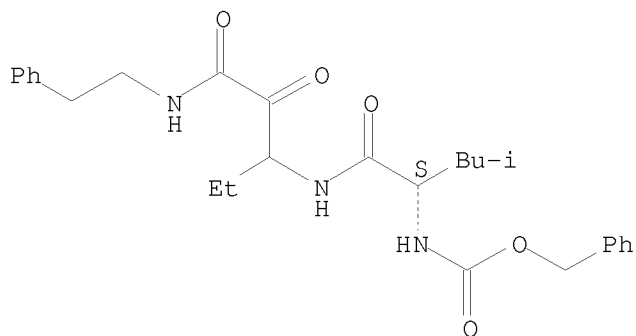
RN 150519-18-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



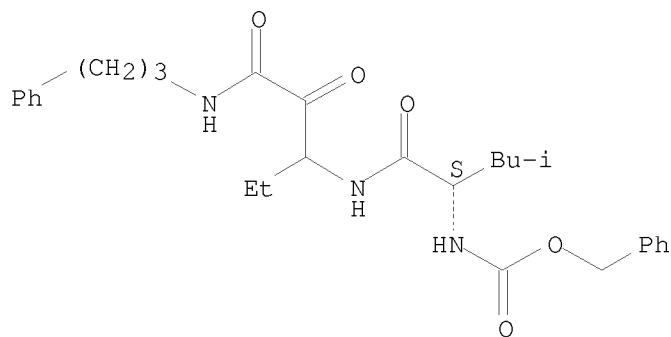
RN 150519-19-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150519-20-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(3-phenylpropyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

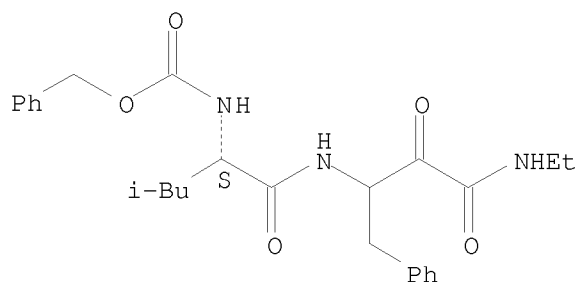
Absolute stereochemistry.



RN 150957-45-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

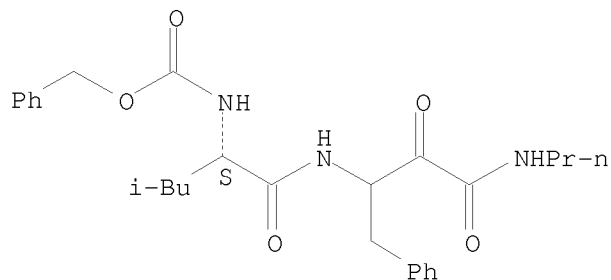
Absolute stereochemistry.



RN 150957-46-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

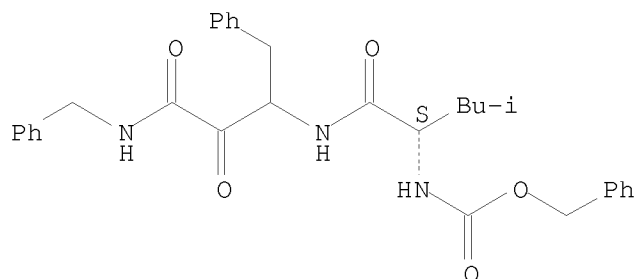
Absolute stereochemistry.



RN 150957-49-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

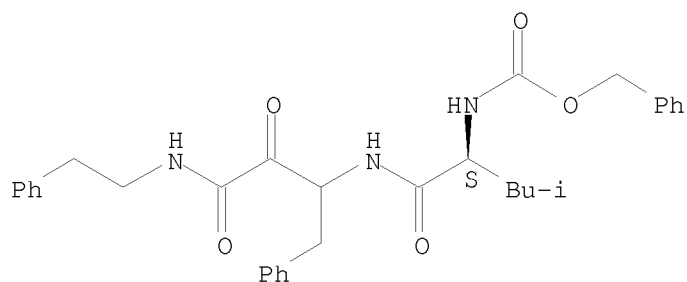
Absolute stereochemistry.



RN 150957-50-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

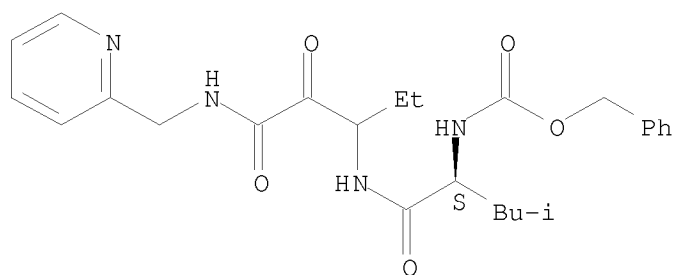
Absolute stereochemistry.



RN 207456-28-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

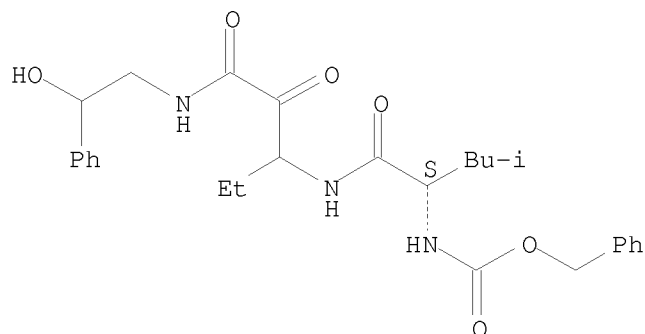
Absolute stereochemistry.



RN 207456-33-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

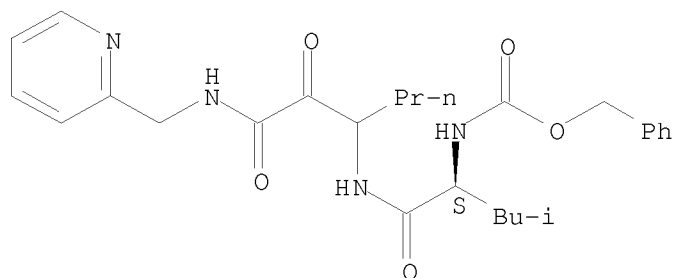
Absolute stereochemistry.



RN 207456-38-0 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[1-[oxo[(2-pyridinylmethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

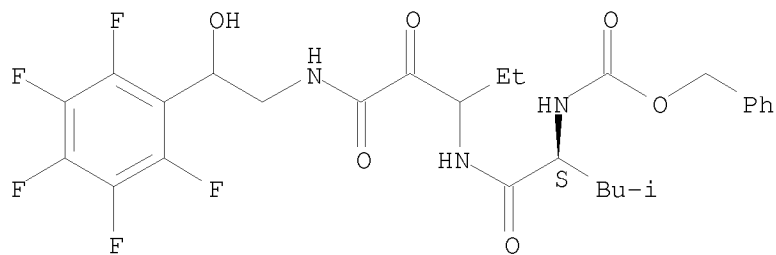
Absolute stereochemistry.



RN 301295-26-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(2,3,4,5,6-pentafluorophenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

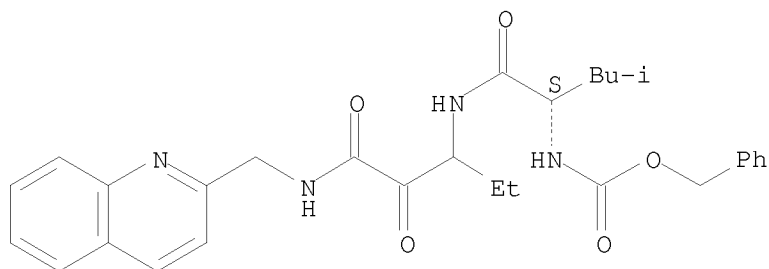
Absolute stereochemistry.



RN 301295-27-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

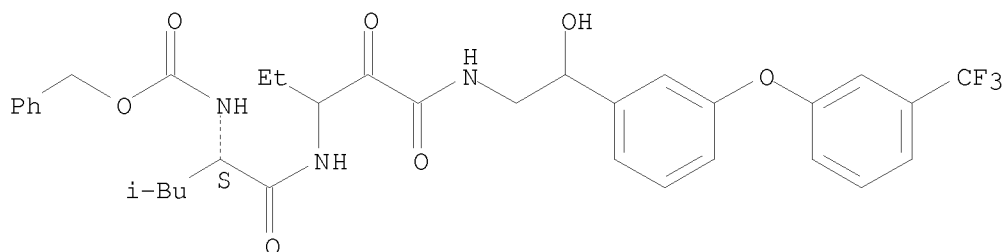
Absolute stereochemistry.



RN 677274-76-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

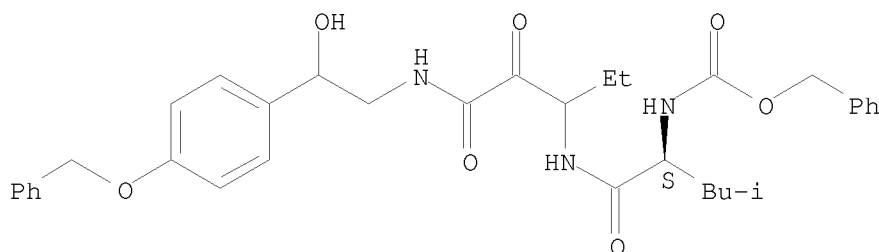
Absolute stereochemistry.



RN 677274-77-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

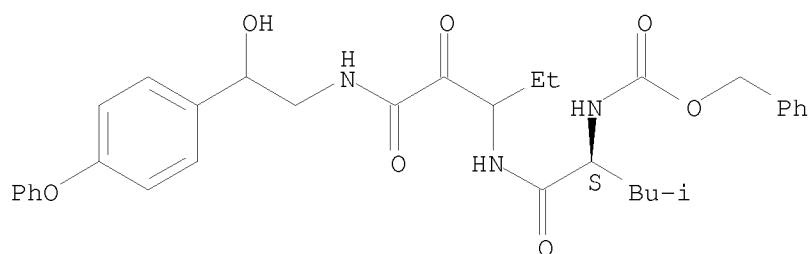


RN 677274-78-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

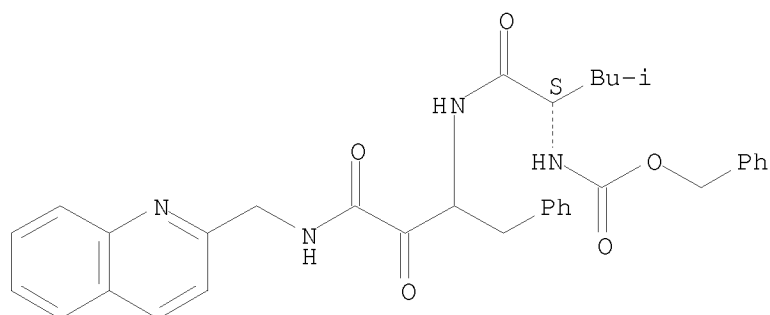




RN 677274-79-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

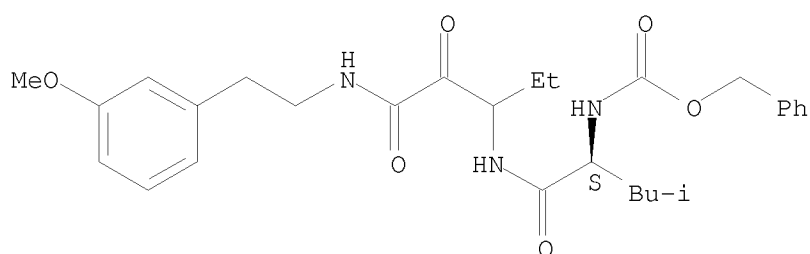
Absolute stereochemistry.



RN 677274-80-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(3-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

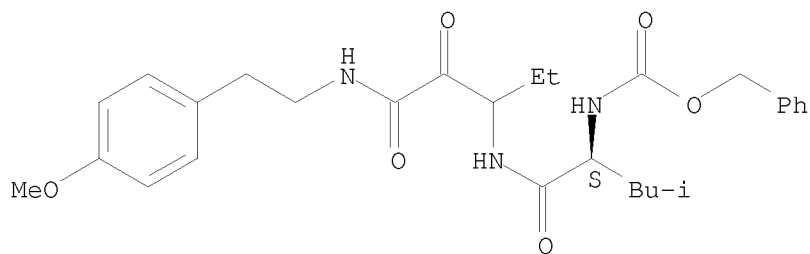
Absolute stereochemistry.



RN 677274-81-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

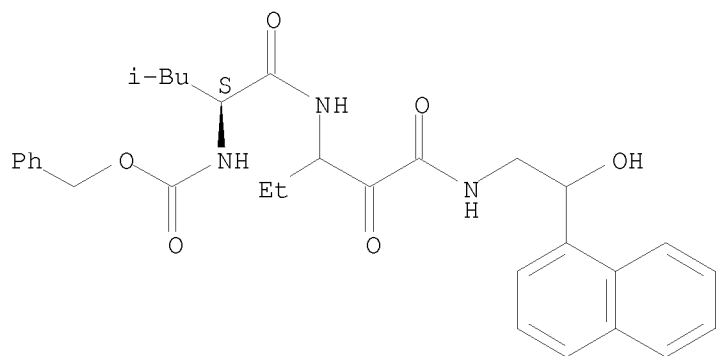
Absolute stereochemistry.



RN 677274-82-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(1-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

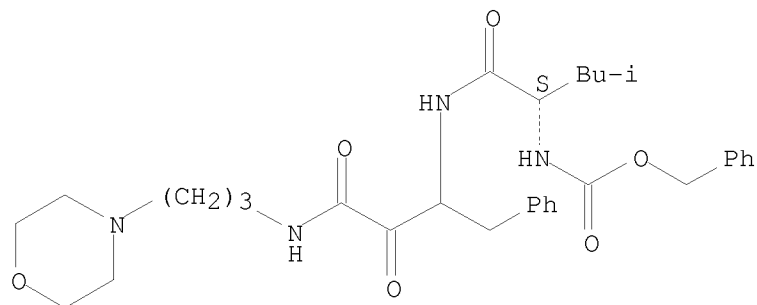
Absolute stereochemistry.



RN 677274-83-8 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

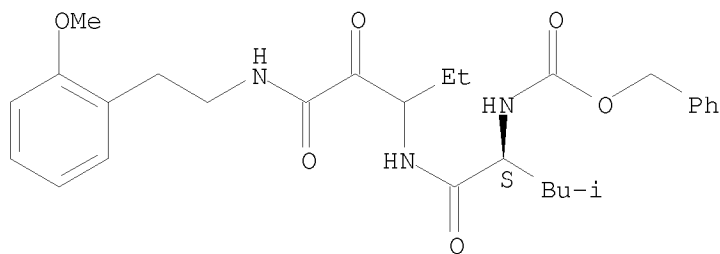
Absolute stereochemistry.



RN 677274-84-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(2-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

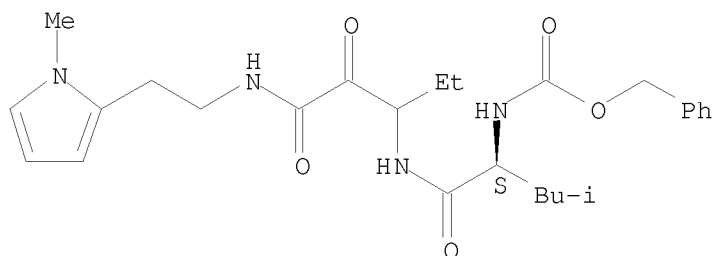
Absolute stereochemistry.



RN 677274-86-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(1-methyl-1H-pyrrol-2-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

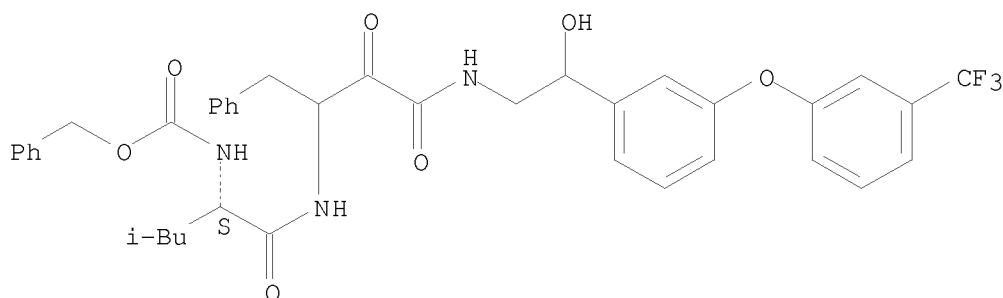
Absolute stereochemistry.



RN 677274-87-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

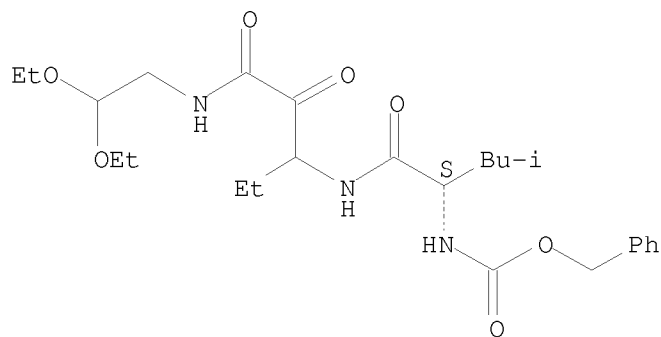
Absolute stereochemistry.



RN 677274-88-3 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid, 11-ethoxy-6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

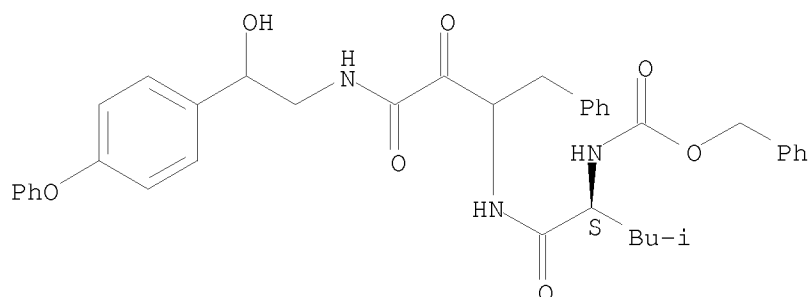
Absolute stereochemistry.



RN 677274-89-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

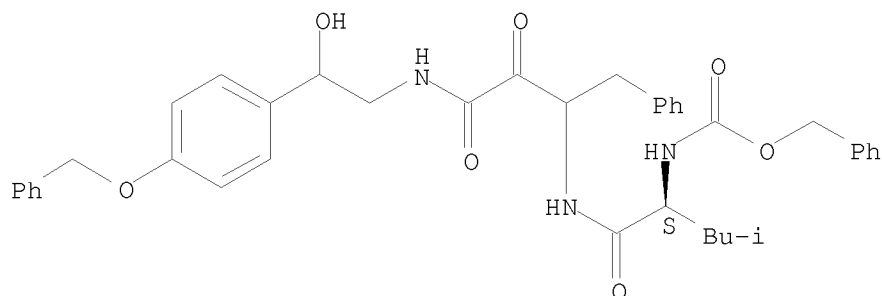
Absolute stereochemistry.



RN 677274-90-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

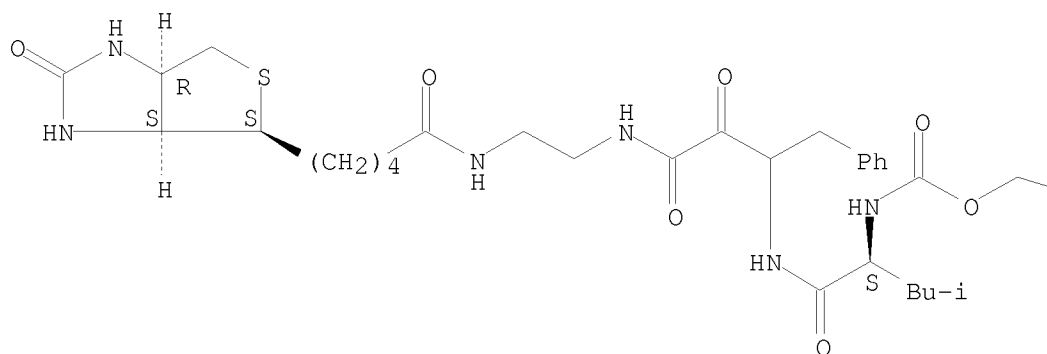


RN 677274-91-8 CAPLUS

CN 2,5,9,12-Tetraazaheptadecanoic acid, 17-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-3-(2-methylpropyl)-4,7,8,13-tetraoxo-6-(phenylmethyl)-, phenylmethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

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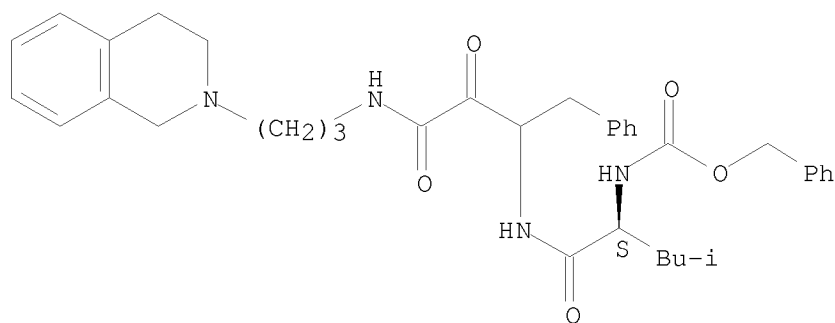


PAGE 1-B

Ph

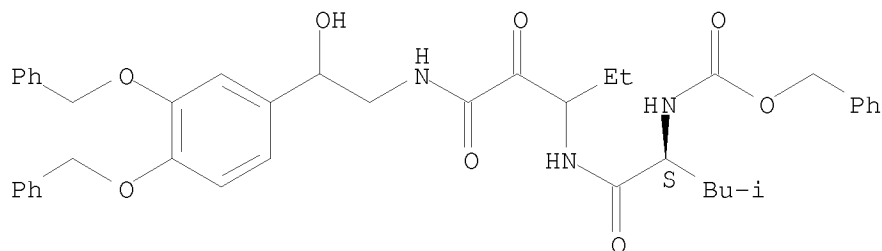
RN 677274-92-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 677274-93-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

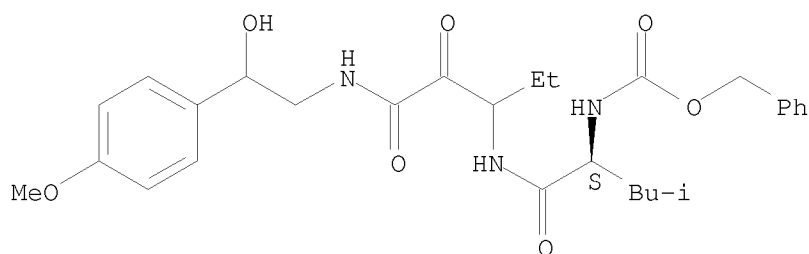
Absolute stereochemistry.



RN 677274-94-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

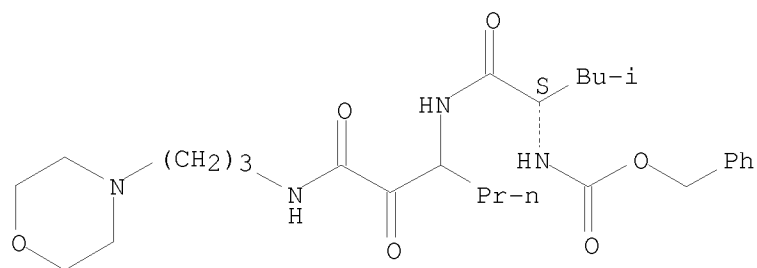
Absolute stereochemistry.



RN 677274-95-2 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[1-[[[3-(4-morpholinyl)propyl]amino]oxoacetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

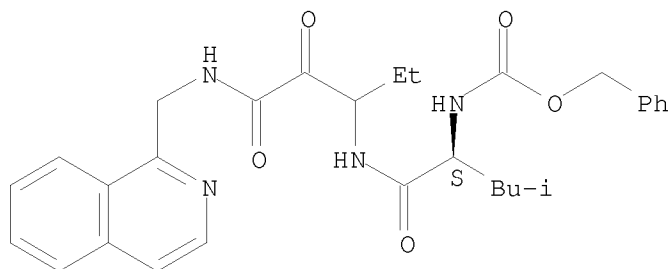
Absolute stereochemistry.



RN 677274-96-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(1-isoquinolinylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

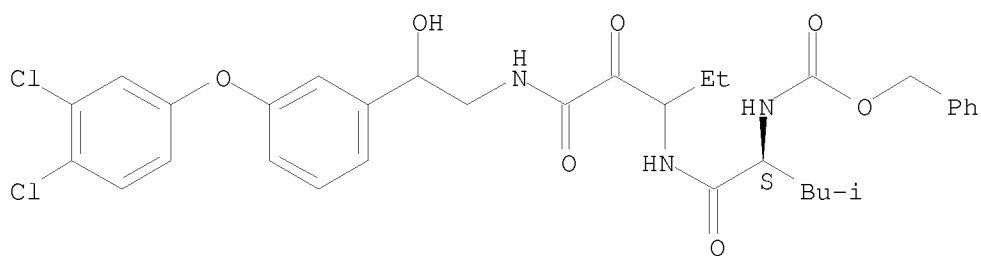
Absolute stereochemistry.



RN 677274-97-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

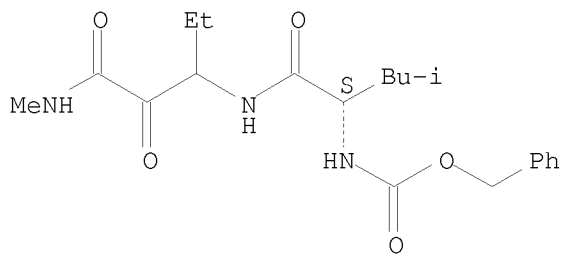
Absolute stereochemistry.



RN 677274-98-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-(methylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

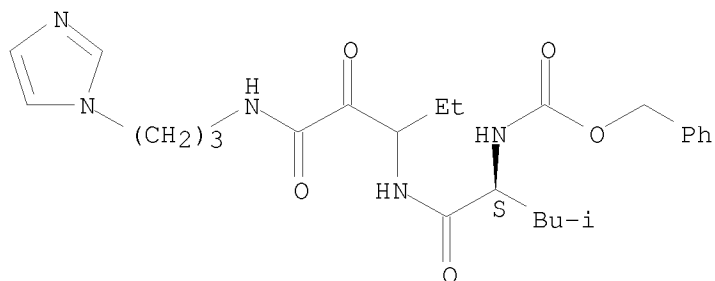
Absolute stereochemistry.



RN 677274-99-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(1H-imidazol-1-yl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

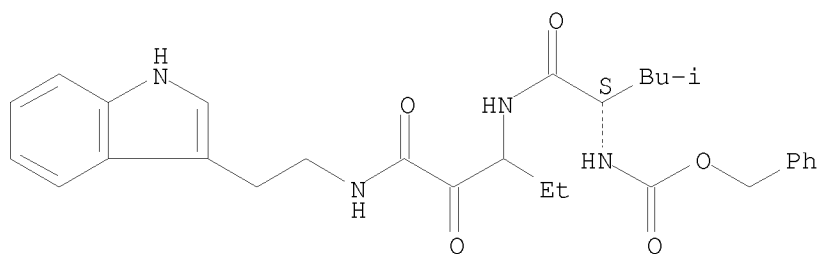
Absolute stereochemistry.



RN 677275-00-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(1H-indol-3-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

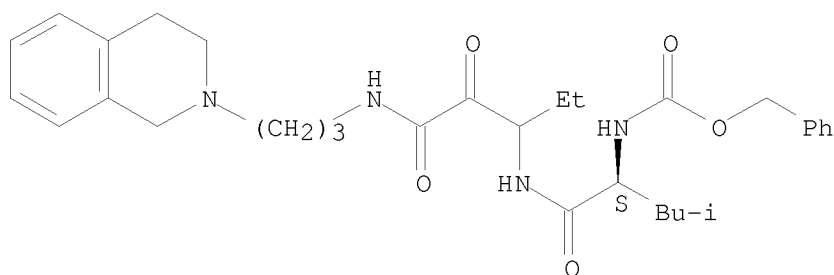
Absolute stereochemistry.



RN 677275-01-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

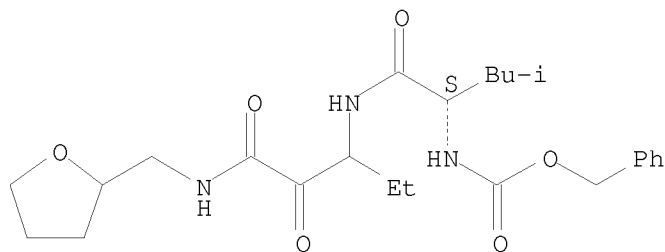


RN 677275-02-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[[tetrahydro-2-furanyl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

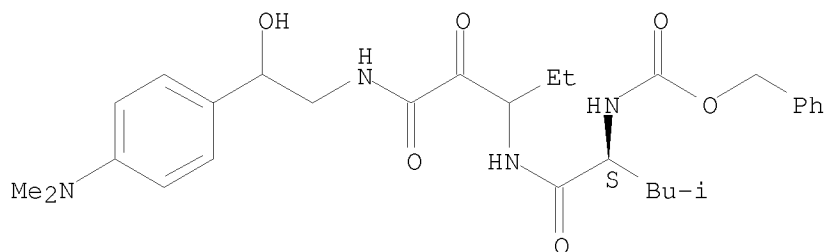




RN 677275-03-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

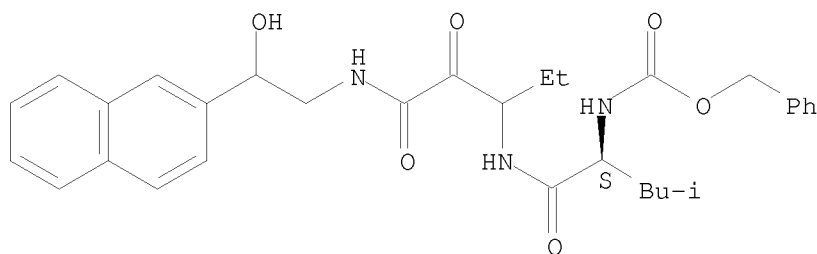
Absolute stereochemistry.



RN 677275-04-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(2-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

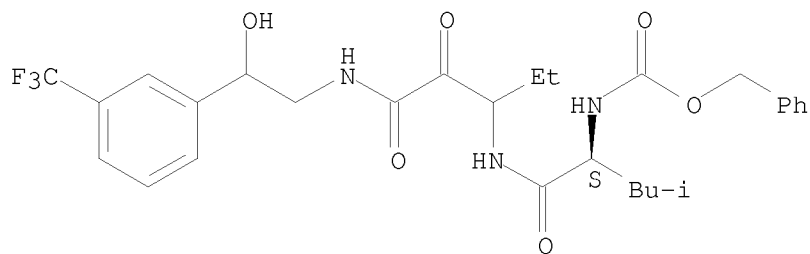
Absolute stereochemistry.



RN 677275-05-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

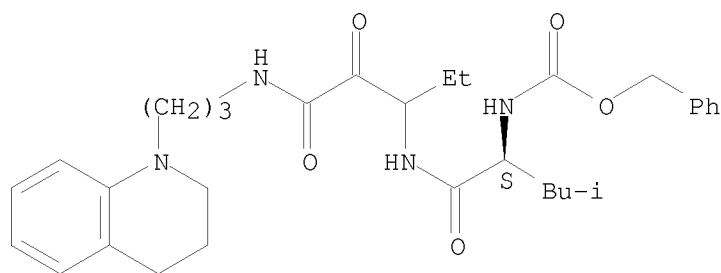
Absolute stereochemistry.



RN 677275-06-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-difluorophenyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

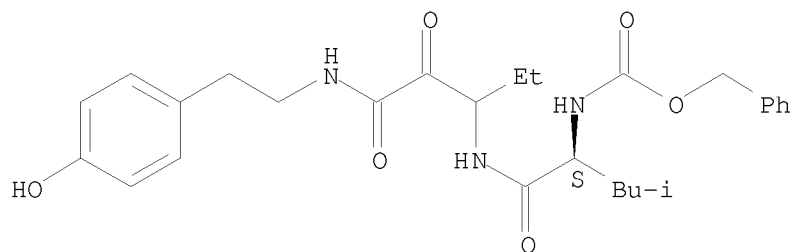
Absolute stereochemistry.



RN 677275-07-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(4-hydroxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

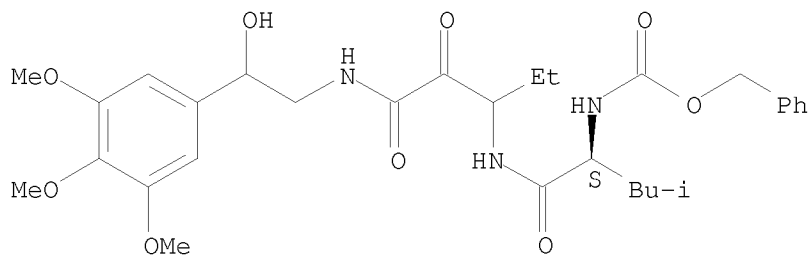
Absolute stereochemistry.



RN 677275-08-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(3,4,5-trimethoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

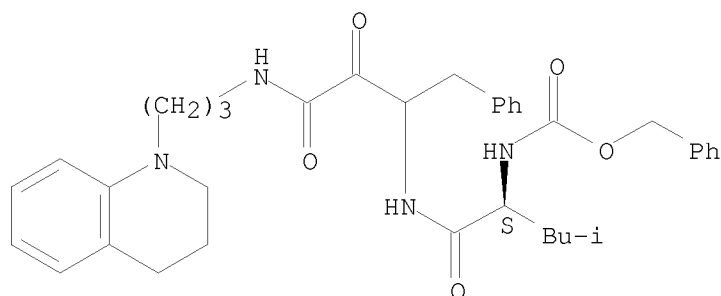
Absolute stereochemistry.



RN 677275-09-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

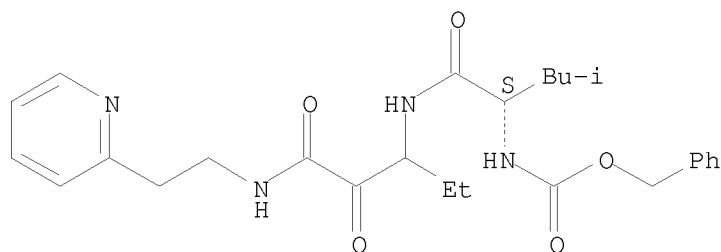
Absolute stereochemistry.



RN 677275-10-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[[2-(2-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

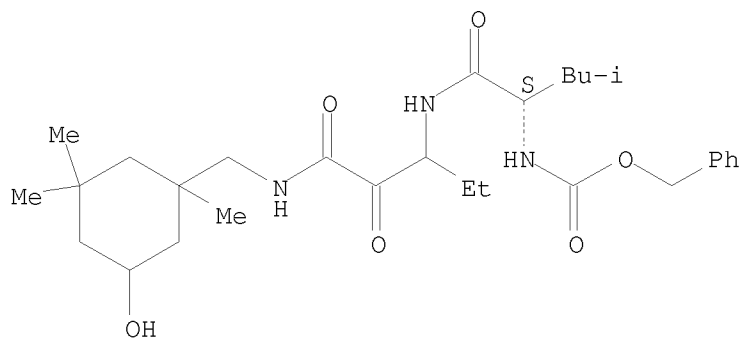
Absolute stereochemistry.



RN 677275-11-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[5-hydroxy-1,3,3-trimethylcyclohexyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

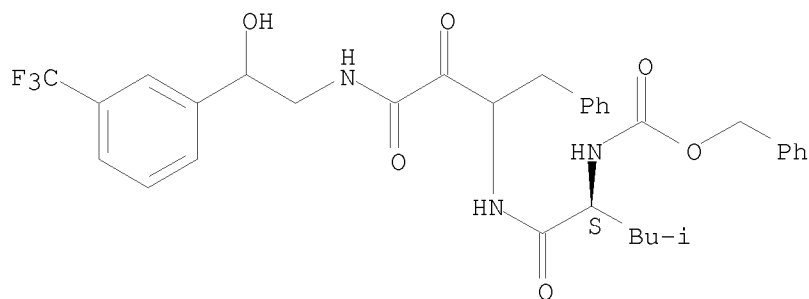
Absolute stereochemistry.



RN 677275-12-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

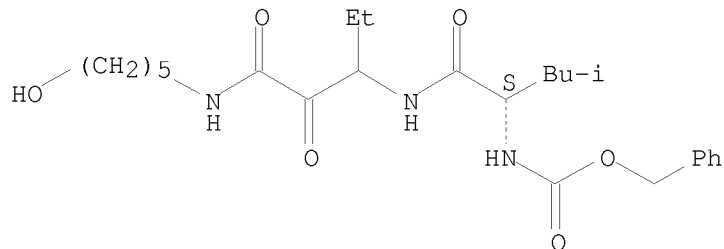
Absolute stereochemistry.



RN 677275-13-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(5-hydroxypentyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

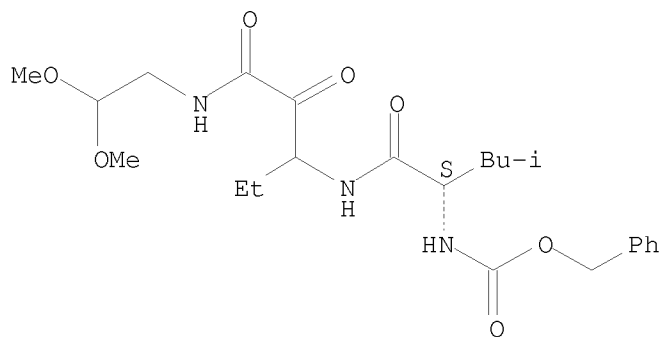
Absolute stereochemistry.



RN 677275-14-8 CAPLUS

CN 12-Oxa-2,5,9-triazatridecanoic acid, 6-ethyl-11-methoxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

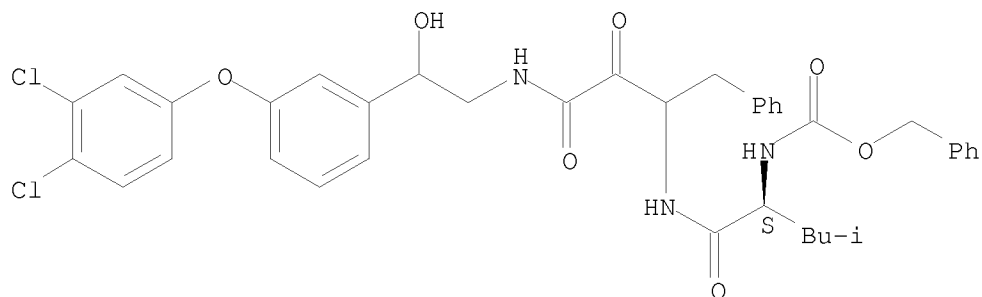
Absolute stereochemistry.



RN 677275-15-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

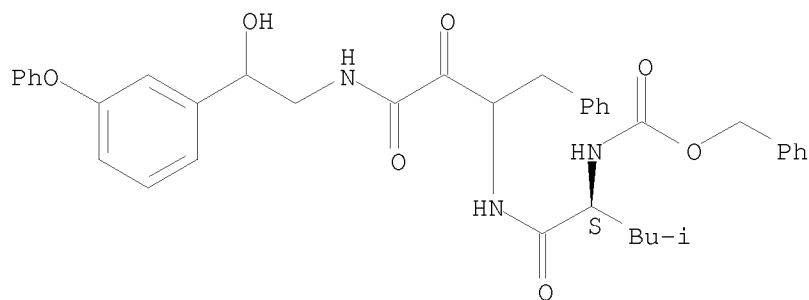
Absolute stereochemistry.



RN 677275-16-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

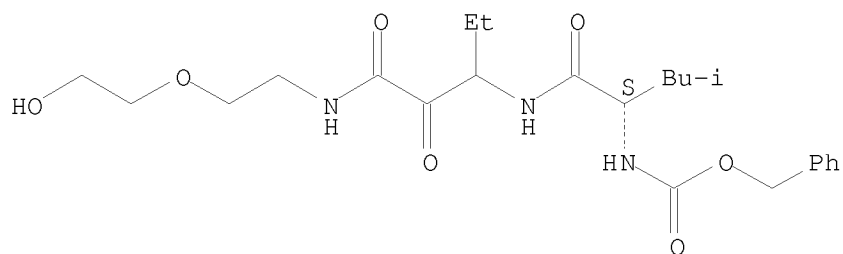
Absolute stereochemistry.



RN 677275-18-2 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid, 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

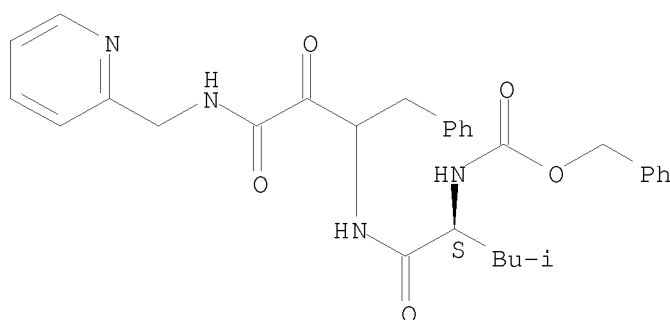
Absolute stereochemistry.



RN 677275-19-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

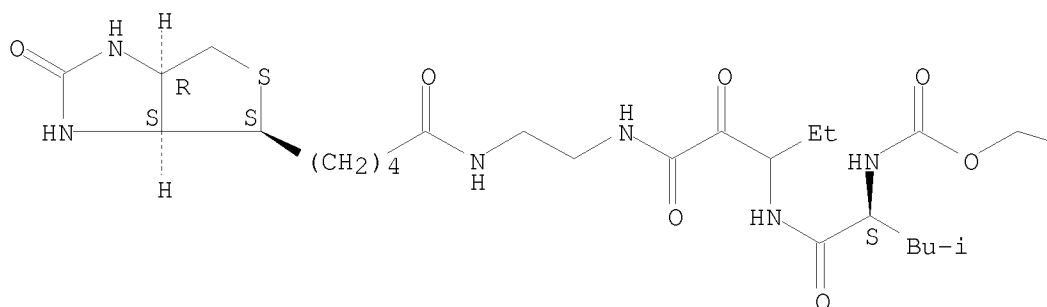


RN 677275-20-6 CAPLUS

CN 2,5,9,12-Tetraazaheptadecanoic acid, 6-ethyl-17-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-3-(2-methylpropyl)-4,7,8,13-tetraoxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

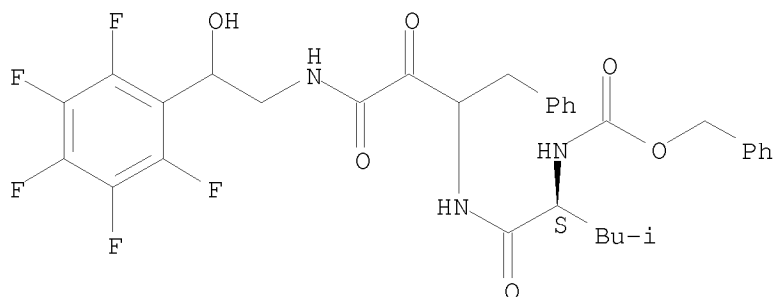


PAGE 1-B

— Ph

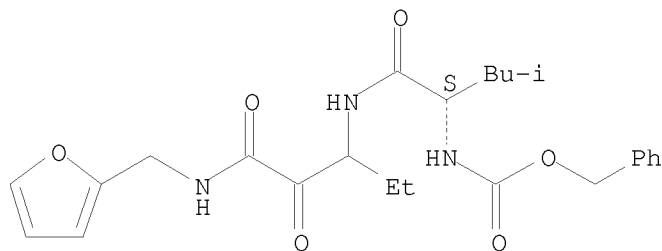
RN 677275-21-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



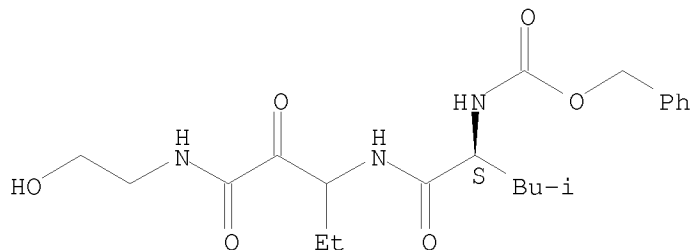
RN 677275-22-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-furanylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



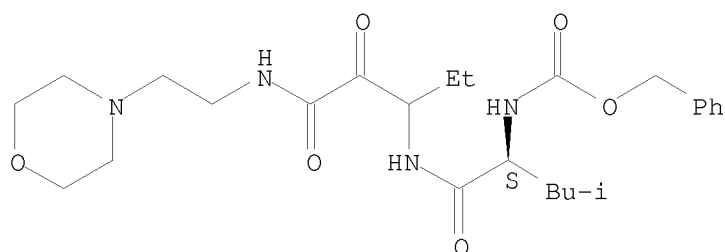
RN 677275-23-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 677275-24-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(4-morpholinyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

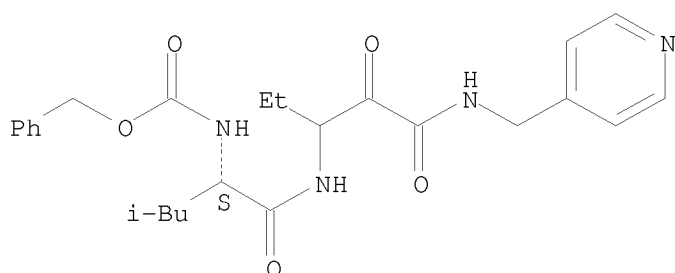
Absolute stereochemistry.



RN 677275-25-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

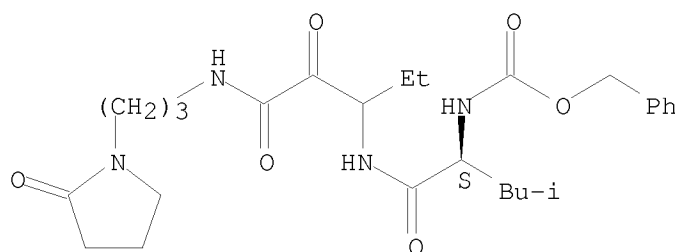
Absolute stereochemistry.



RN 677275-26-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

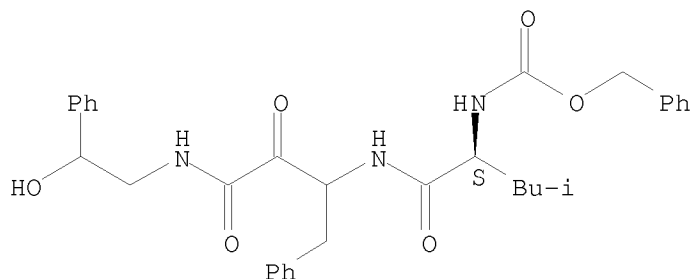


RN 677275-27-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

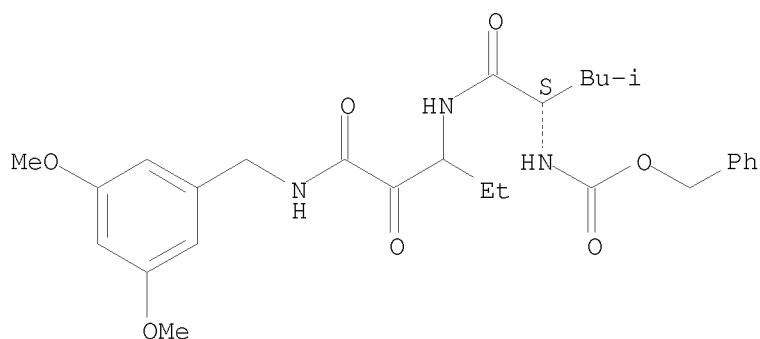




RN 677275-28-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

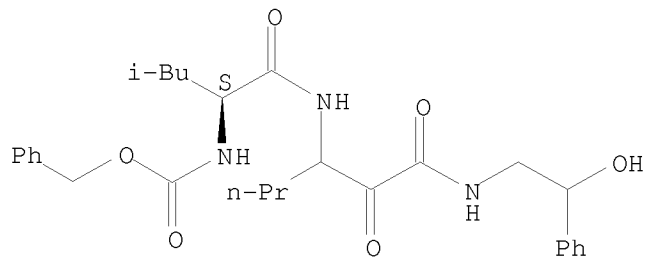
Absolute stereochemistry.



RN 677275-29-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-[(2-hydroxy-2-phenylethyl)amino]oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

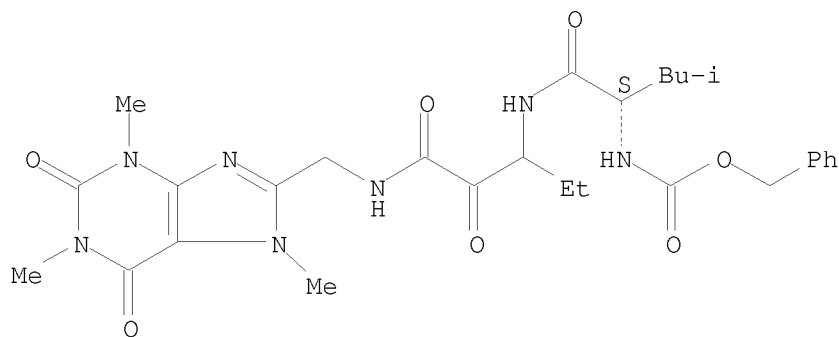
Absolute stereochemistry.



RN 677275-30-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

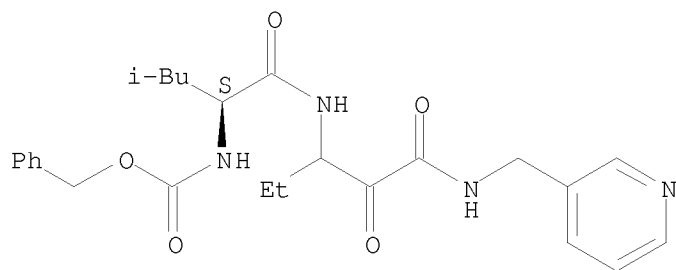
Absolute stereochemistry.



RN 677275-31-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(3-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

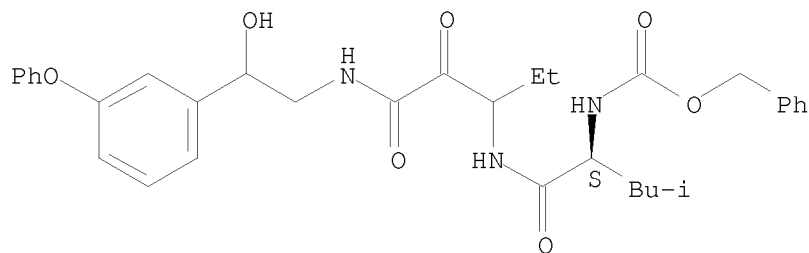
Absolute stereochemistry.



RN 677275-32-0 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (CA INDEX NAME)

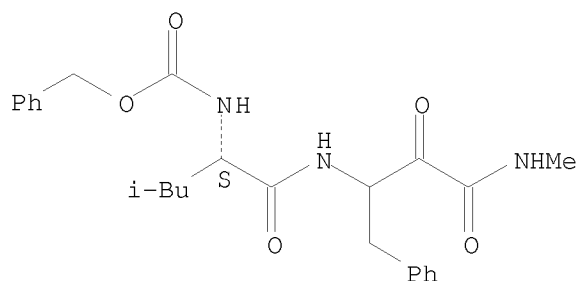
Absolute stereochemistry.



RN 904299-60-1 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[3-(methylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

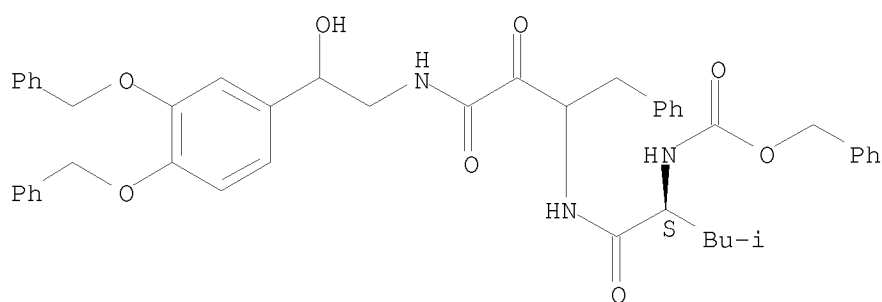
Absolute stereochemistry.



RN 904299-61-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

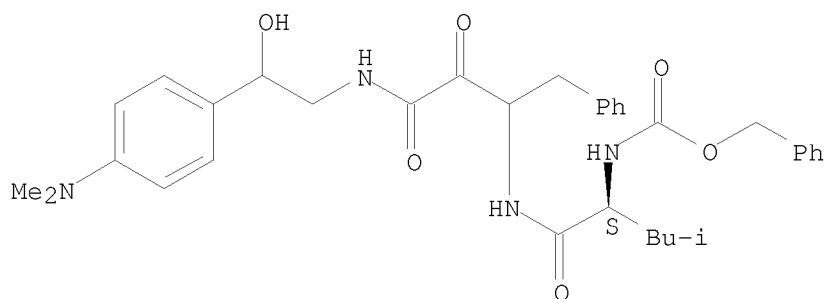
Absolute stereochemistry.



RN 904299-62-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr l10 2-39

L10 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:409063 CAPLUS

DOCUMENT NUMBER: 144:404435

TITLE: Protease inhibitor prodrug compounds and kits for treating muscle disorders and methods of use thereof

INVENTOR(S): Stracher, Alfred; Kesner, Leo; Barton, Norman W.;  
 Carver, Theodore E.  
 PATENT ASSIGNEE(S): Ceptor Corporation, USA  
 SOURCE: PCT Int. Appl., No pp. given  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005124563	A2	20051229	WO 2005-US20903	20050613 <--
WO 2005124563	A3	20081002		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AP, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, EA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, EP, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, OA, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20080039531	A1	20080214	US 2005-321782	20051228
PRIORITY APPLN. INFO.:			US 2004-578914P	P 20040612 <--
			US 2004-633274P	P 20041203 <--
			WO 2005-US20903	A2 20050613

OTHER SOURCE(S): MARPAT 144:404435

AB The invention describes protease inhibitor prodrug compds. and kits for treating muscle disorders, as well as and methods for their use. Studies with aminocarnitylsuccinylleucylarginal and its di-Et acetal are presented.

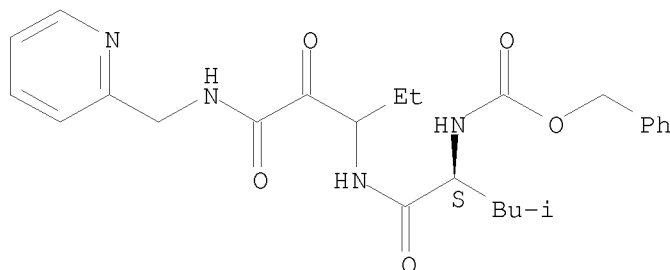
IT 207456-28-8D, carrier conjugates 207456-33-5D, carrier conjugates 677274-85-0D, carrier conjugates

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, carrier conjugates; protease inhibitor prodrugs for treating muscle disorders)

RN 207456-28-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

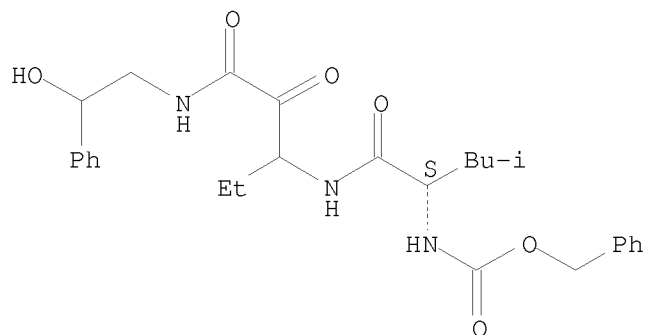


RN 207456-33-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA

INDEX NAME)

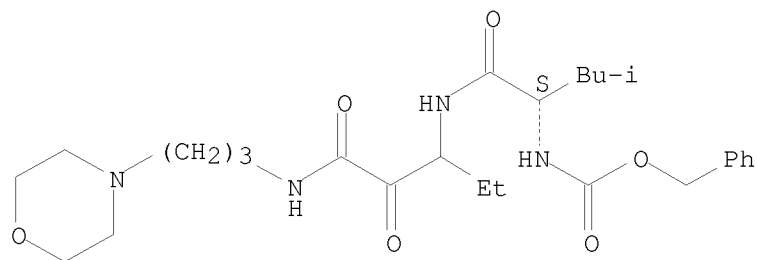
Absolute stereochemistry.



RN 677274-85-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:540563 CAPLUS

DOCUMENT NUMBER: 143:60256

TITLE: Preparation of leucyl  $\alpha$ -ketoamide derivatives as calpain inhibitors

INVENTOR(S): Shirasaki, Yoshihisa; Miyashita, Hiroyuki; Nakamura, Masayuki; Inoue, Jun

PATENT ASSIGNEE(S): Senju Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

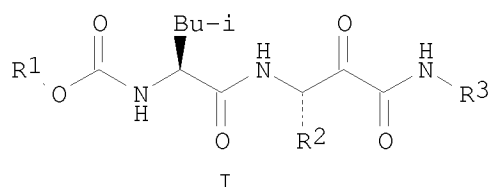
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056519	A1	20050623	WO 2004-JP18692	20041208 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,			

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG

JP 2006076989 A 20060323 JP 2004-354908 20041208 <--  
 EP 1692098 A1 20060823 EP 2004-807051 20041208 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS  
 CN 1890210 A 20070103 CN 2004-80036672 20041208 <--  
 IN 2006KN01379 A 20070504 IN 2006-KN1379 20060523 <--  
 US 20070004643 A1 20070104 US 2006-582015 20060607 <--  
 PRIORITY APPLN. INFO.: JP 2003-415764 A 20031212 <--  
 JP 2004-234164 A 20040811 <--  
 WO 2004-JP18692 W 20041208

OTHER SOURCE(S): CASREACT 143:60256; MARPAT 143:60256  
 GI



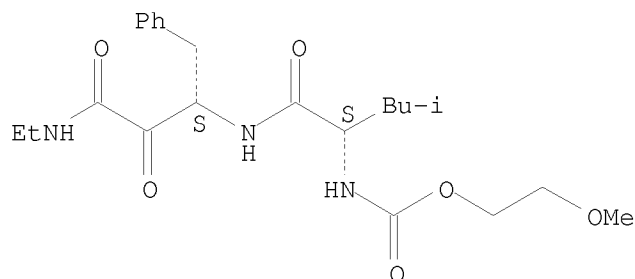
AB The invention provides compds. I (R1 is alkyl, alkoxy- or heterocyclylalkyl or heterocyclyl; R2 is alkyl or phenylalkyl; R3 is H, alkyl, halo-, alkoxy- or phenylalkyl or fused polycyclyl), which have potent calpain inhibitory activity, are well absorbed orally and produce good drug levels in blood. Thus, I (R1 = MeOCH2CH2, R2 = PhCH2, R3 = Et) was prepared via peptide coupling reaction and shown to strongly inhibit  $\mu$ -calpain and m-calpain (IC50 = 0.17 and 0.11 uM, resp.).

IT 854402-43-0P 854402-46-3P 854402-49-6P  
 854402-50-9P 854402-51-0P 854402-52-1P  
 854402-53-2P 854402-54-3P 854402-55-4P  
 854402-57-6P 854402-59-8P 854402-60-1P  
 854402-61-2P 854402-62-3P 854402-63-4P  
 854402-64-5P 854402-65-6P 854402-66-7P  
 854402-67-8P 854402-68-9P 854402-69-0P  
 854402-70-3P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of leucyl  $\alpha$ -ketoamide derivs. as calpain inhibitors)

RN 854402-43-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

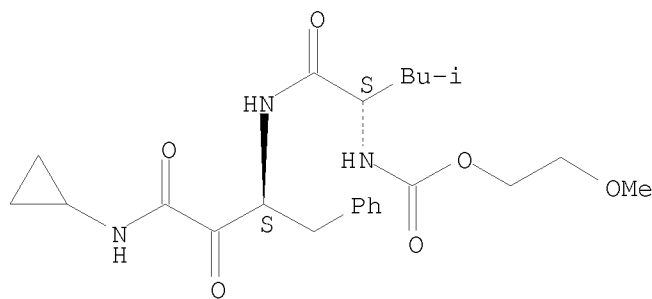
Absolute stereochemistry.



RN 854402-46-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

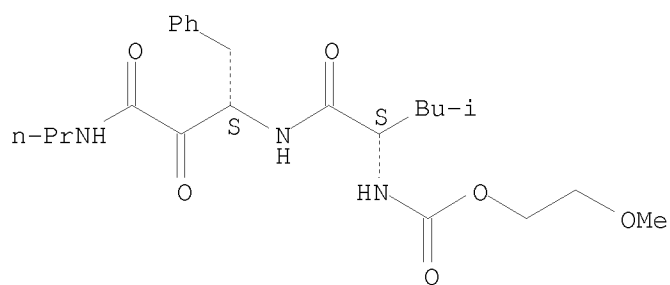
Absolute stereochemistry. Rotation (+).



RN 854402-49-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

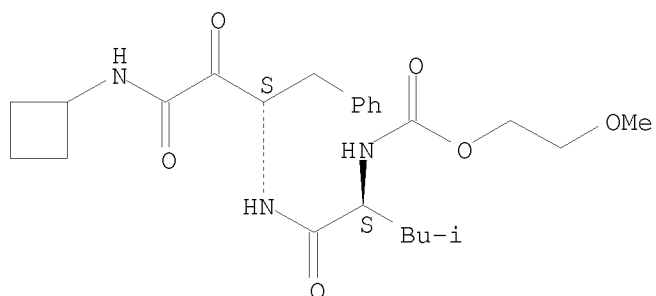
Absolute stereochemistry.



RN 854402-50-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclobutylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

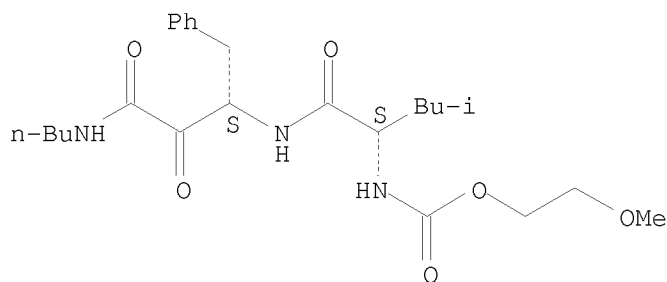
Absolute stereochemistry.



RN 854402-51-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

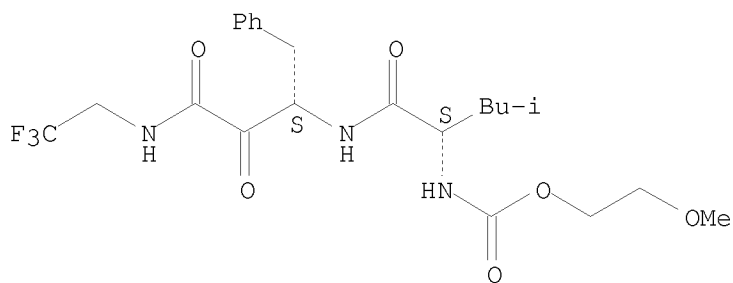
Absolute stereochemistry.



RN 854402-52-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(2,2,2-trifluoroethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

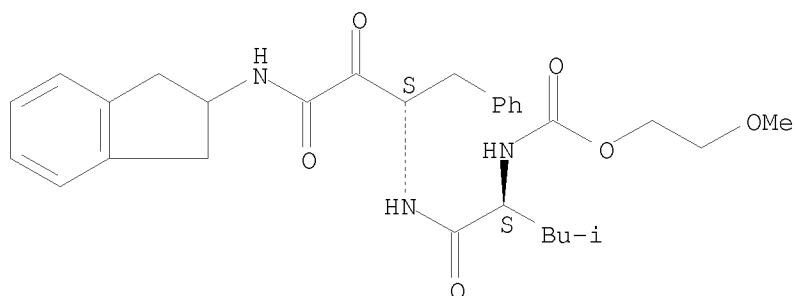


RN 854402-53-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-[(2,3-dihydro-1H-inden-2-yl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

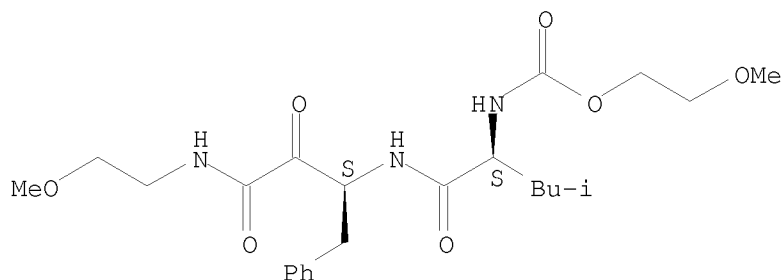
Absolute stereochemistry.





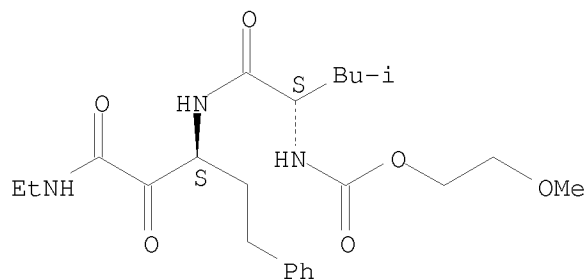
RN 854402-54-3 CAPLUS  
 CN 12-Oxa-2,5,9-triazatridecanoic acid,  
 3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, 2-methoxyethyl ester,  
 (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



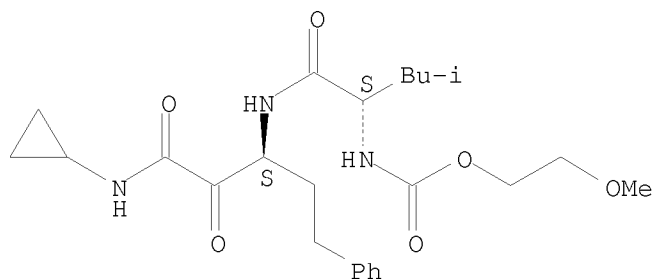
RN 854402-55-4 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(2-phenylethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 854402-57-6 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(2-phenylethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester  
 (9CI) (CA INDEX NAME)

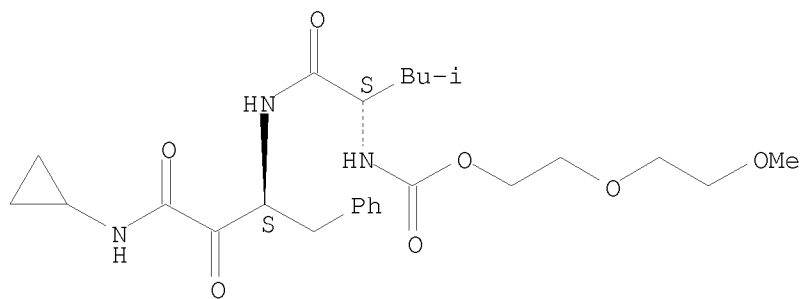
Absolute stereochemistry.



RN 854402-59-8 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-methoxyethoxy)ethyl ester (CA INDEX NAME)

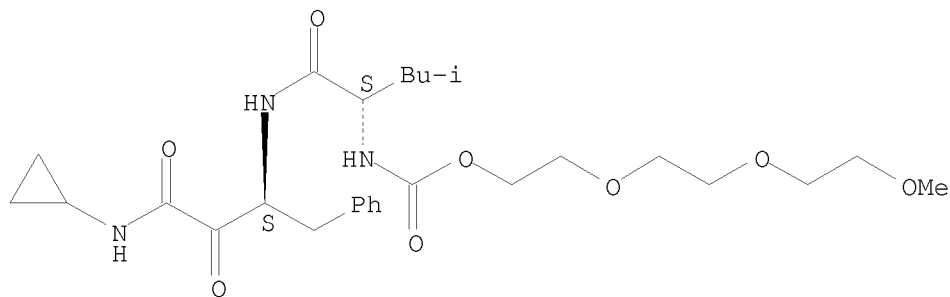
Absolute stereochemistry. Rotation (+).



RN 854402-60-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

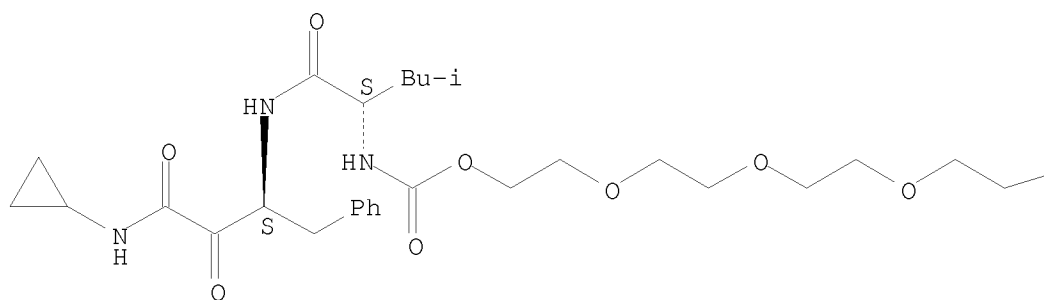


RN 854402-61-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 3,6,9,12-tetraoxatridec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



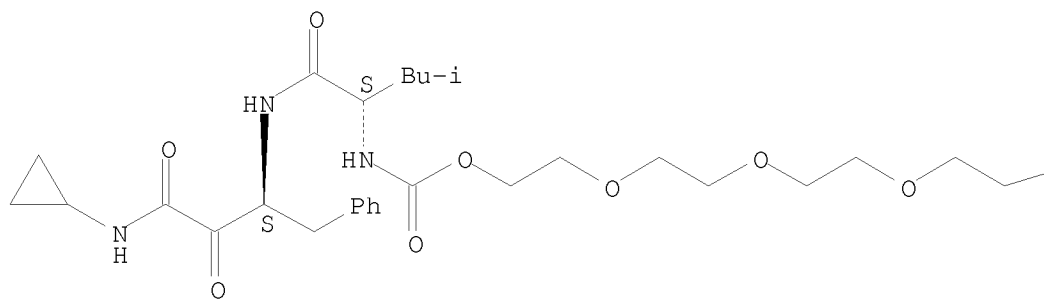
PAGE 1-B

OMe

RN 854402-62-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 3,6,9,12,15-pentaoxahehexadec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

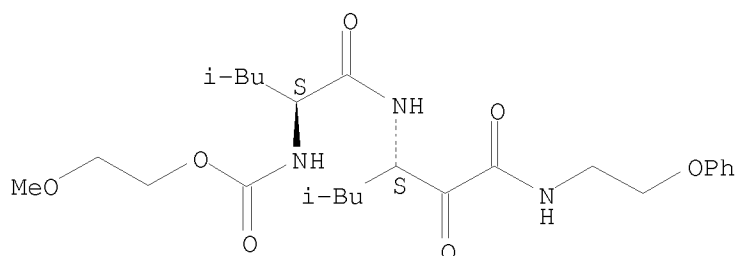


PAGE 1-B

OMe

RN 854402-63-4 CAPLUS  
 CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-methyl-1-[oxo[(2-phenoxyethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

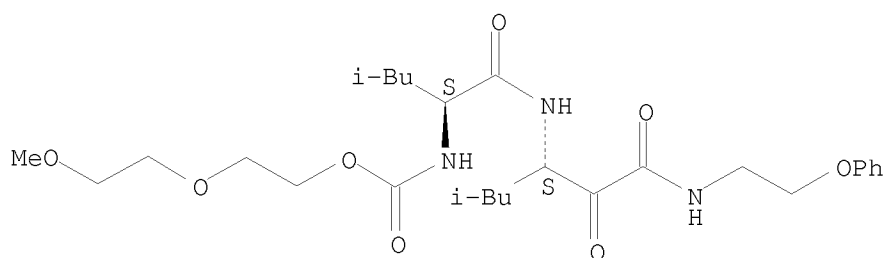
Absolute stereochemistry.



RN 854402-64-5 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-methyl-1-[oxo[(2-phenoxyethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, 2-(2-methoxyethoxy)ethyl ester (9CI) (CA INDEX NAME)

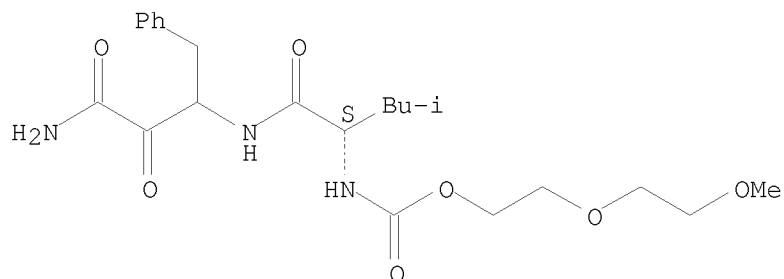
Absolute stereochemistry.



RN 854402-65-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-amino-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-methoxyethoxy)ethyl ester (9CI) (CA INDEX NAME)

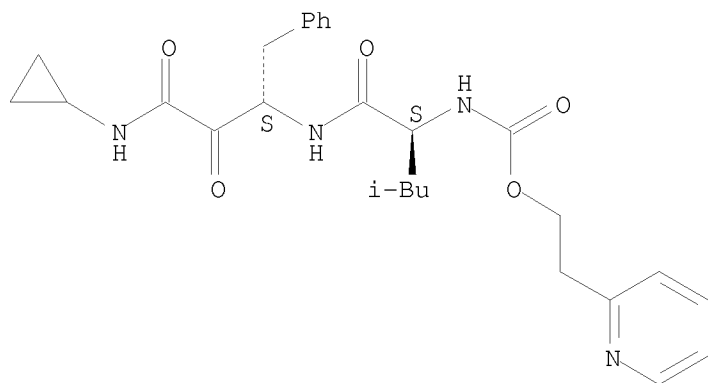
Absolute stereochemistry.



RN 854402-66-7 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-pyridinyl)ethyl ester (CA INDEX NAME)

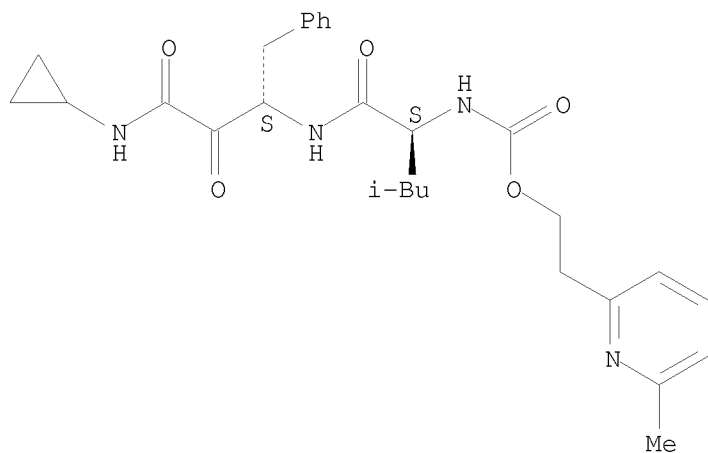
Absolute stereochemistry. Rotation (-).



RN 854402-67-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(6-methyl-2-pyridinyl)ethyl ester (9CI) (CA INDEX NAME)

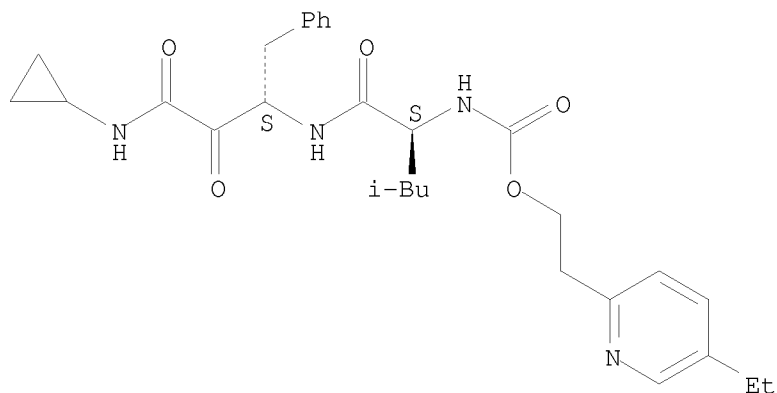
Absolute stereochemistry. Rotation (-).



RN 854402-68-9 CAPLUS

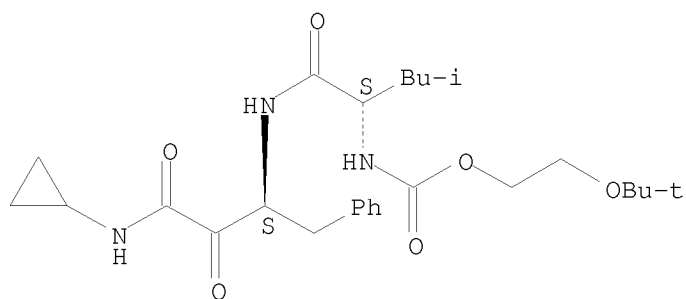
CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(5-ethyl-2-pyridinyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



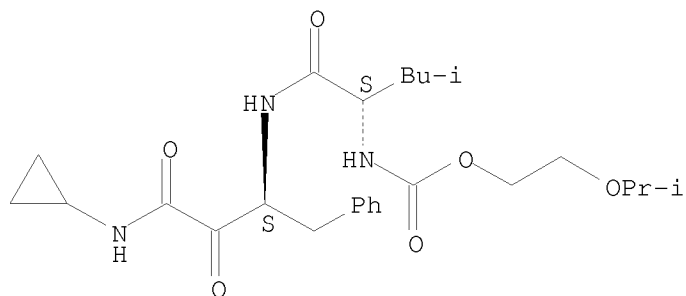
RN 854402-69-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(1,1-dimethylethoxy)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 854402-70-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(1-methylethoxy)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2004:290471 CAPLUS

DOCUMENT NUMBER: 140:315086  
 TITLE: Peptide ketoamide inhibitors for the treatment of neuropathies and hyperproliferative disorders  
 INVENTOR(S): Powers, James C.; Glass, Jonathan D.  
 PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA  
 SOURCE: PCT Int. Appl., 56 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004028466	A2	20040408	WO 2003-US30449	20030925 <--
WO 2004028466	A3	20041007		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003299084	A1	20040419	AU 2003-299084	20030925 <--
US 20040127427	A1	20040701	US 2003-671360	20030925 <--
US 7429560	B2	20080930		
EP 1553964	A2	20050720	EP 2003-756875	20030925 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006503069	T	20060126	JP 2004-539997	20030925 <--
PRIORITY APPLN. INFO.:			US 2002-413506P	P 20020925 <--
			WO 2003-US30449	W 20030925 <--

OTHER SOURCE(S): MARPAT 140:315086

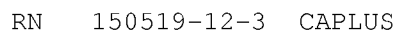
AB Compns. and methods for treating neural pathologies are provided. In particular, compns. and methods for treating neural pathologies including axonal degeneration are provided. The compns. include peptide  $\alpha$ -ketoamides optionally in combination with a second therapeutic agent. Another aspect of the invention provides compns. and methods for treating hyperproliferative disorders. Exemplary compns. for treating hyperproliferative disorders include an antiproliferative agent such as paclitaxel, in combination with a calpain inhibitor such as AK295.

IT 150519-09-8 150519-12-3 150519-18-9  
 150519-19-0 150519-20-3 150957-45-2  
 150957-46-3 150957-49-6 150957-50-9  
 207456-28-8 207456-33-5 207456-38-0  
 301295-26-1 301295-27-2 677274-76-9  
 677274-77-0 677274-78-1 677274-79-2  
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 677274-83-8 677274-84-9 677274-85-0  
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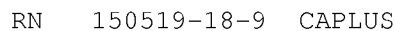
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

RN 150519-09-8 CAPLUS

Absolute stereochemistry.

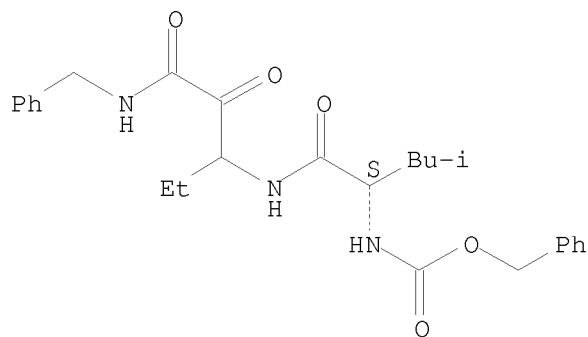


Absolute stereochemistry.



Absolute stereochemistry.

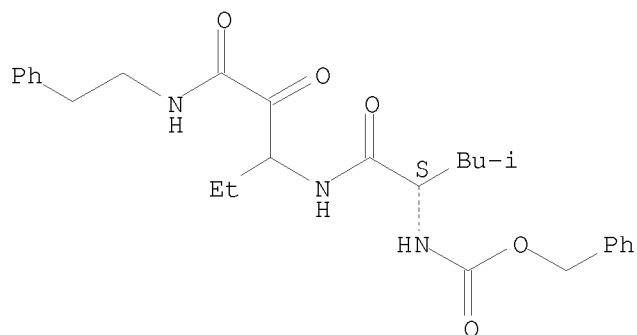




RN 150519-19-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

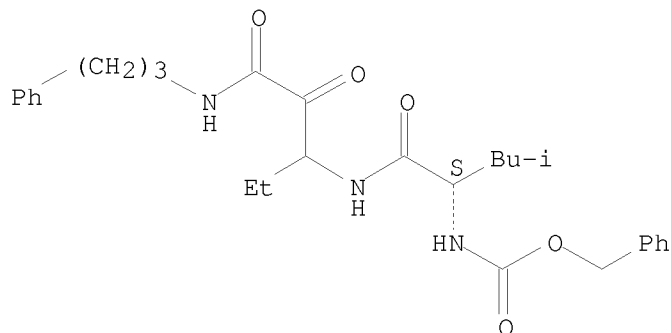
Absolute stereochemistry.



RN 150519-20-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(3-phenylpropyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

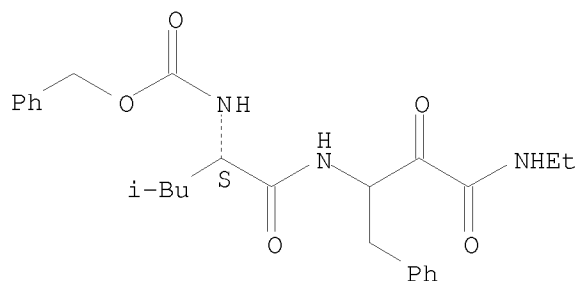
Absolute stereochemistry.



RN 150957-45-2 CAPLUS

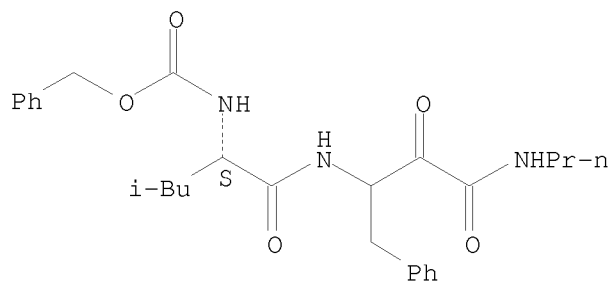
CN Carbamic acid, [(1S)-1-[[[3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



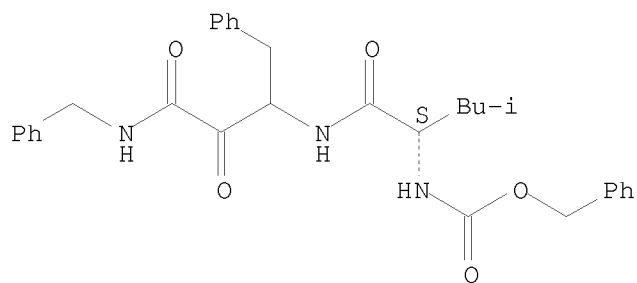
RN 150957-46-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



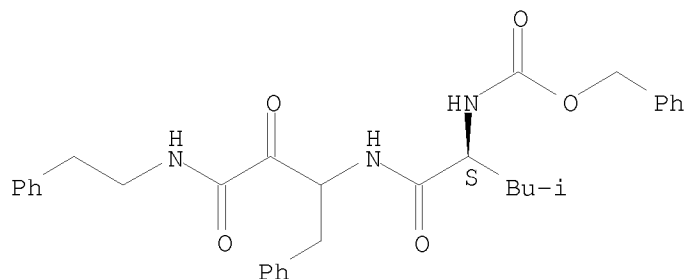
RN 150957-49-6 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-(phenylmethylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 150957-50-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

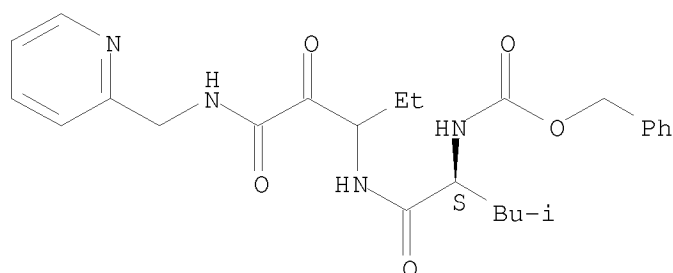
Absolute stereochemistry.



RN 207456-28-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

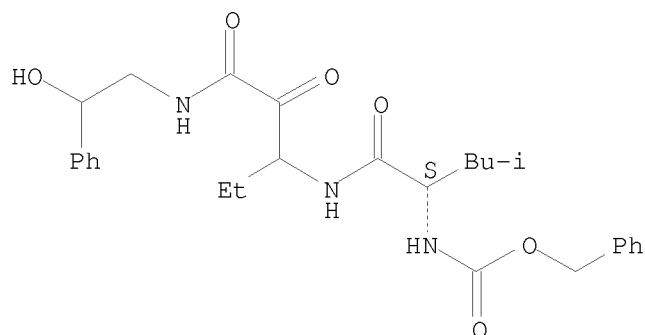
Absolute stereochemistry.



RN 207456-33-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

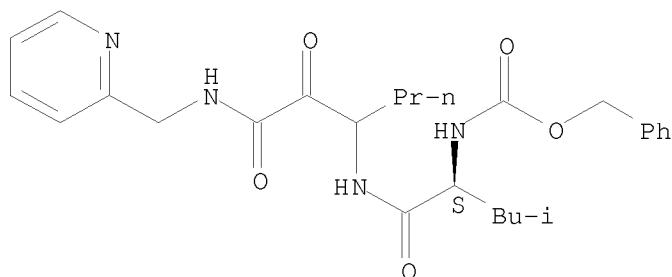
Absolute stereochemistry.



RN 207456-38-0 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[1-[oxo[(2-pyridinylmethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

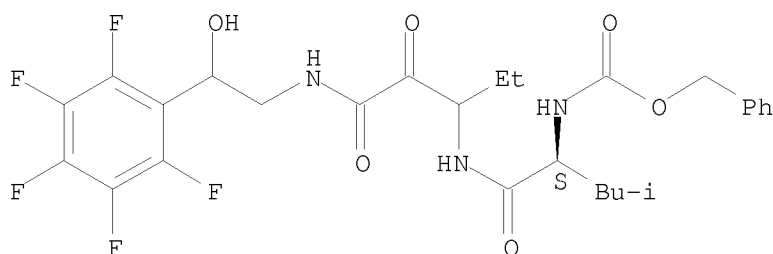
Absolute stereochemistry.



RN 301295-26-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(2,3,4,5,6-pentafluorophenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

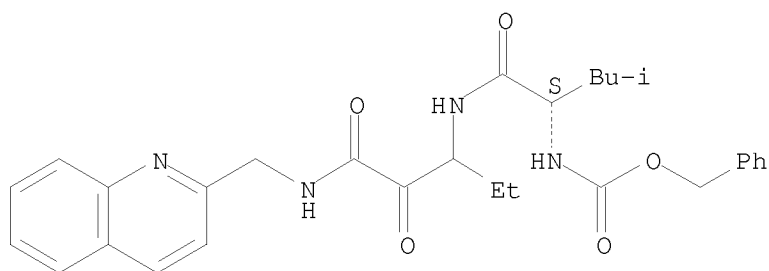
Absolute stereochemistry.



RN 301295-27-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

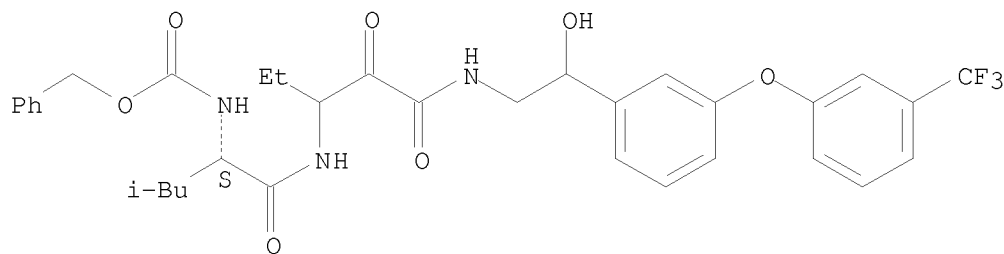
Absolute stereochemistry.



RN 677274-76-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

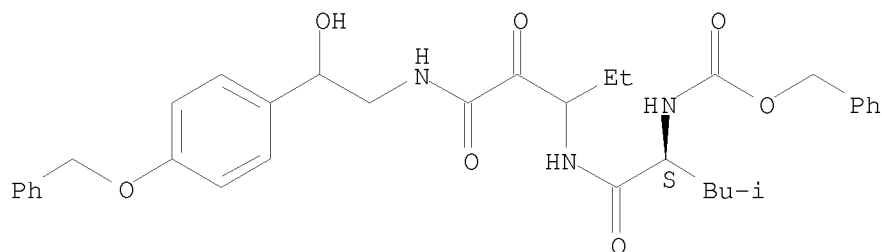
Absolute stereochemistry.



RN 677274-77-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

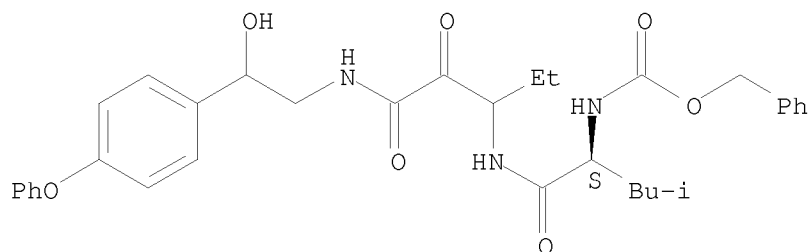
Absolute stereochemistry.



RN 677274-78-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

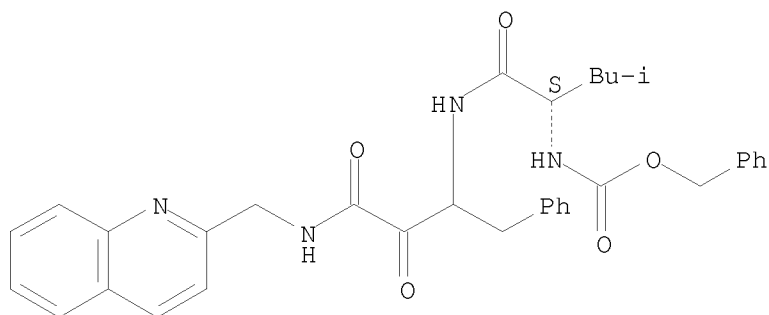
Absolute stereochemistry.



RN 677274-79-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

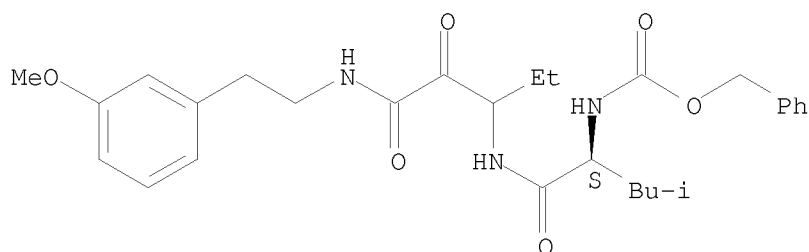
Absolute stereochemistry.



RN 677274-80-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(3-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

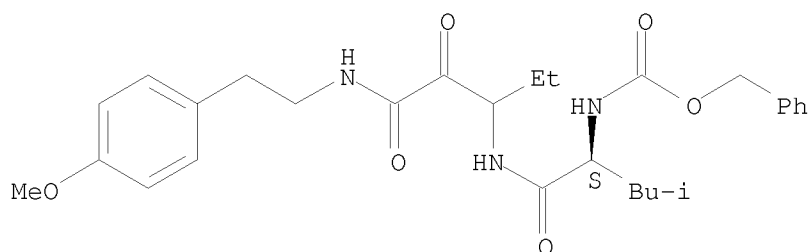
Absolute stereochemistry.



RN 677274-81-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

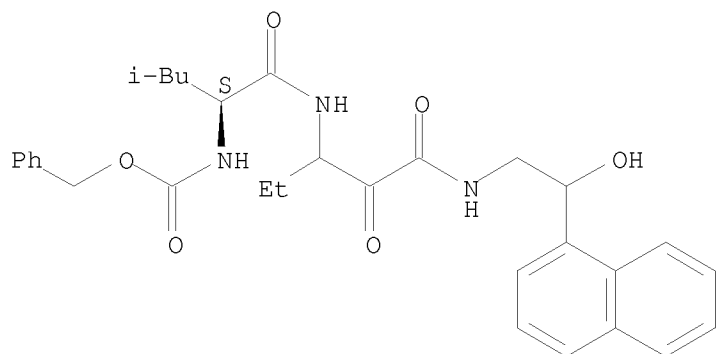
Absolute stereochemistry.



RN 677274-82-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(1-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

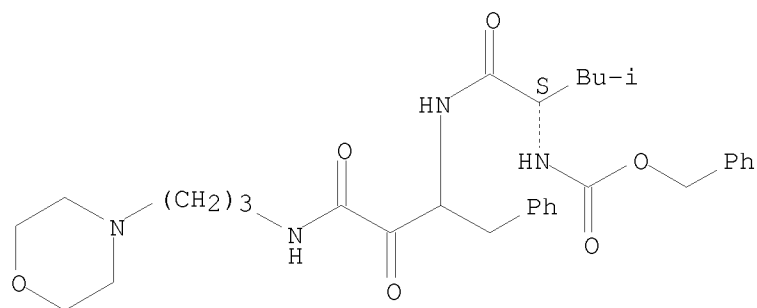
Absolute stereochemistry.



RN 677274-83-8 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

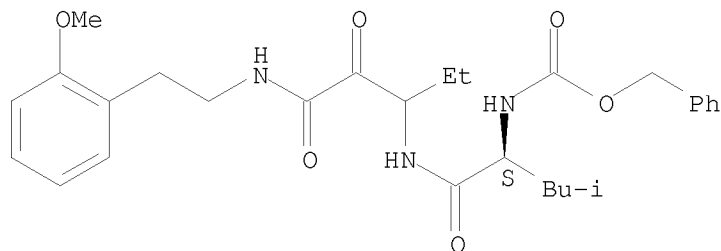
Absolute stereochemistry.



RN 677274-84-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(2-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

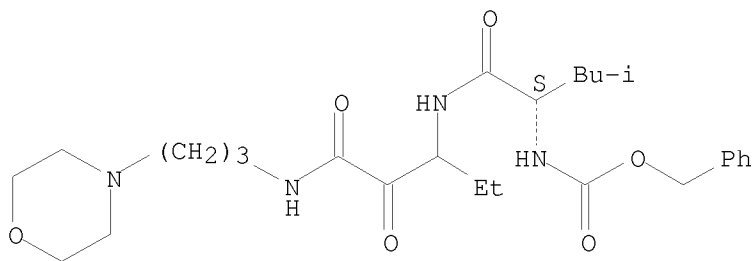
Absolute stereochemistry.



RN 677274-85-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

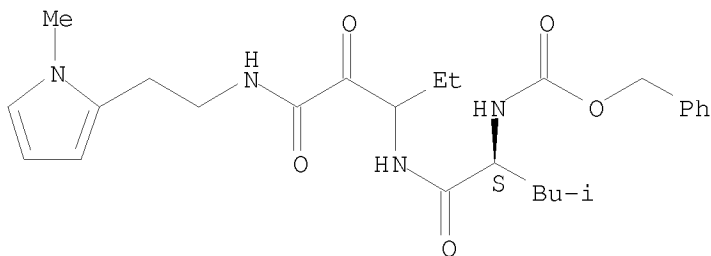
Absolute stereochemistry.



RN 677274-86-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(1-methyl-1H-pyrrol-2-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

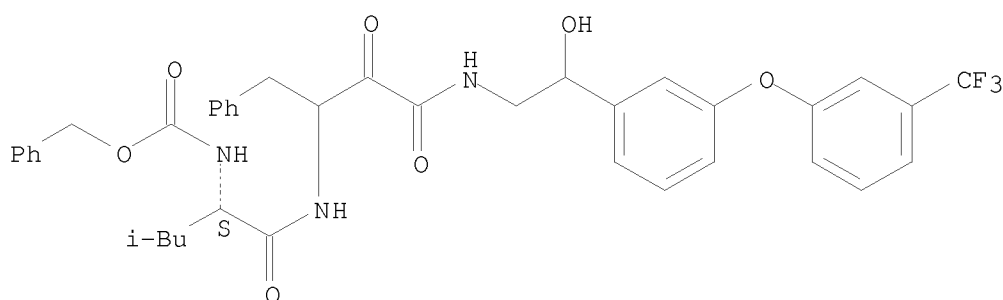
Absolute stereochemistry.



RN 677274-87-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

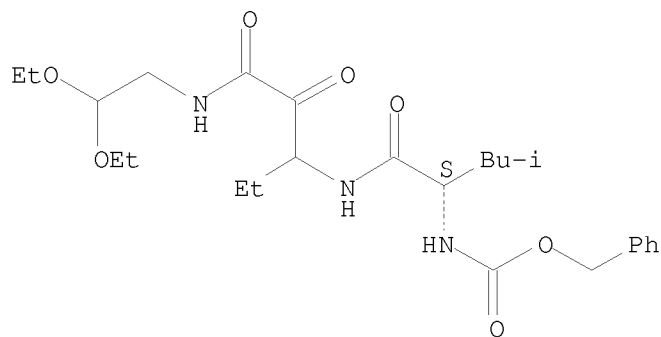


RN 677274-88-3 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid, 11-ethoxy-6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

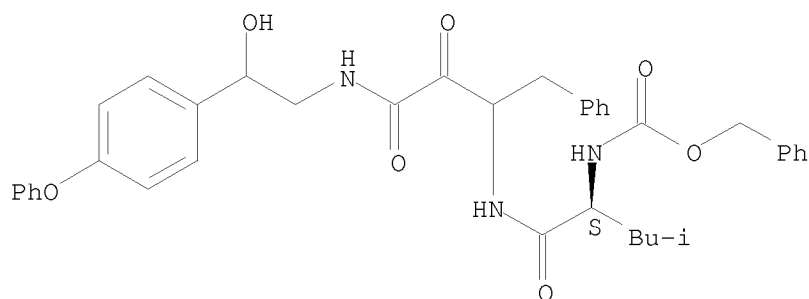




RN 677274-89-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

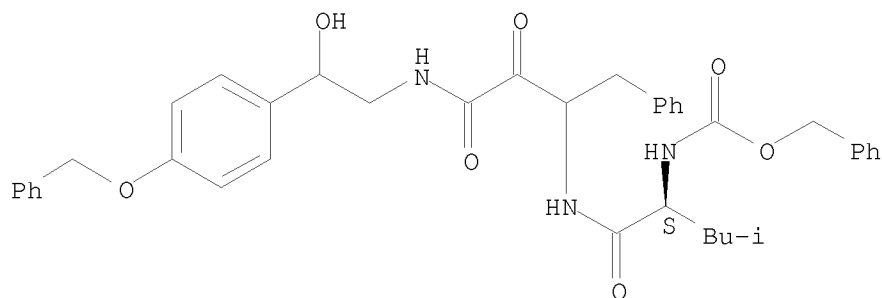
Absolute stereochemistry.



RN 677274-90-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

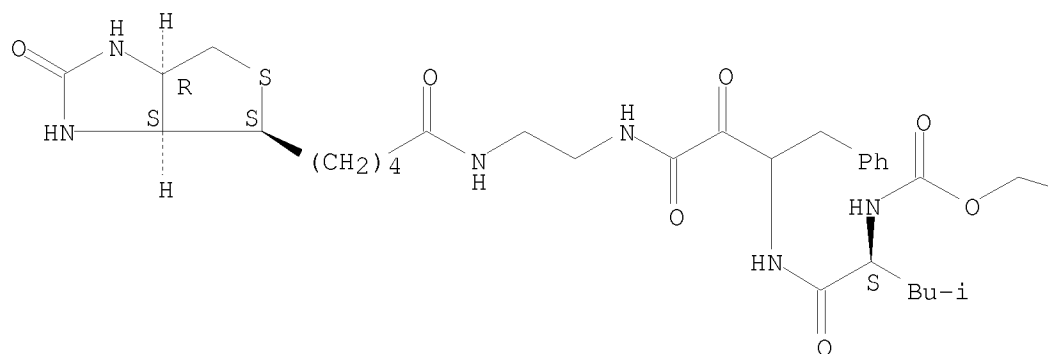


RN 677274-91-8 CAPLUS

CN 2,5,9,12-Tetraazaheptadecanoic acid, 17-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-3-(2-methylpropyl)-4,7,8,13-tetraoxo-6-(phenylmethyl)-, phenylmethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

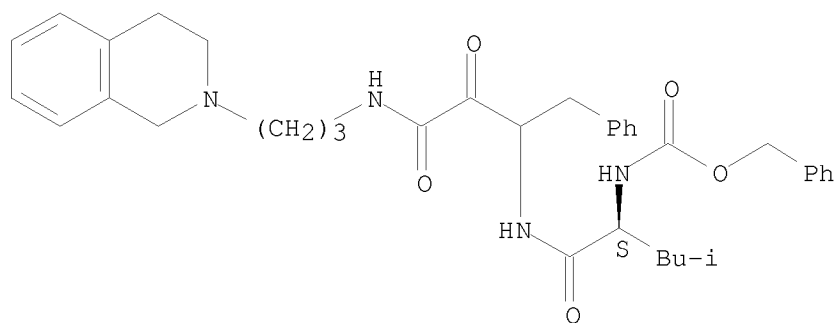


PAGE 1-B

Ph

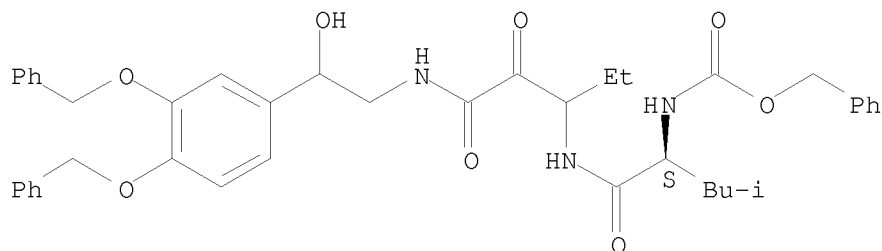
RN 677274-92-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 677274-93-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

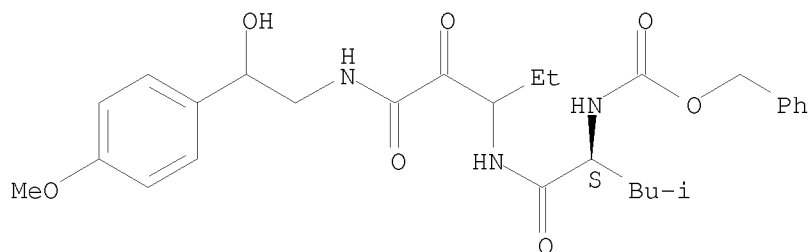
Absolute stereochemistry.



RN 677274-94-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

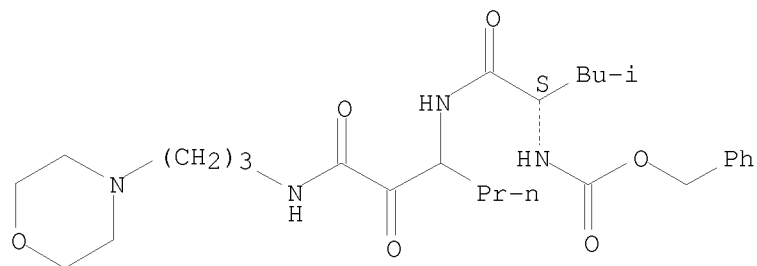
Absolute stereochemistry.



RN 677274-95-2 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[1-[[[3-(4-morpholinyl)propyl]amino]oxoacetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

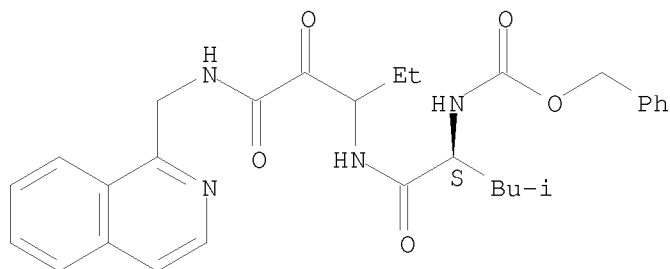
Absolute stereochemistry.



RN 677274-96-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(1-isoquinolinylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

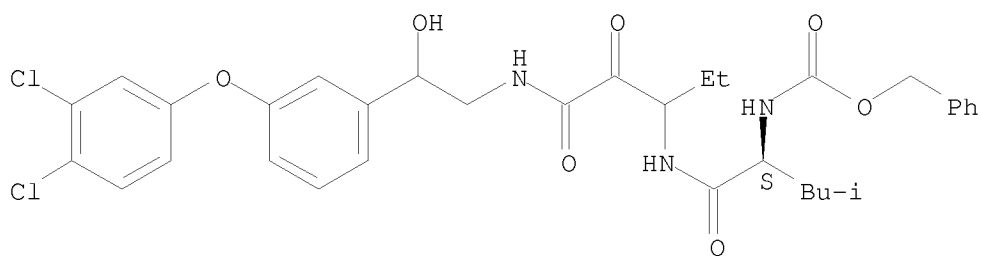
Absolute stereochemistry.



RN 677274-97-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

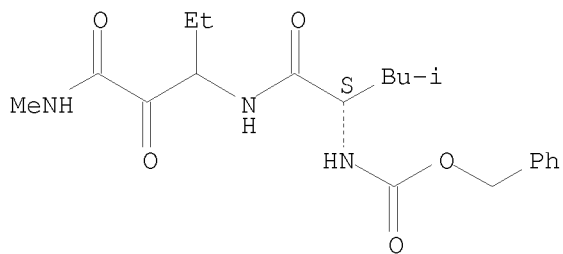
Absolute stereochemistry.



RN 677274-98-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-(methylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

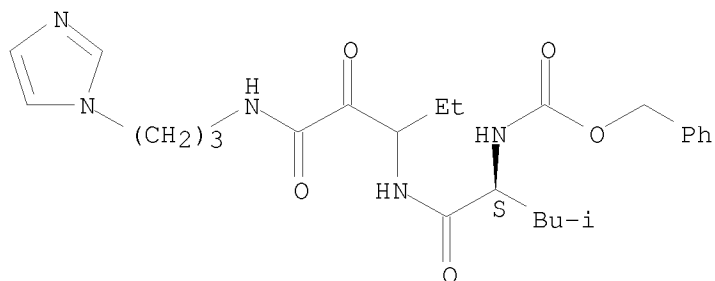
Absolute stereochemistry.



RN 677274-99-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(1H-imidazol-1-yl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

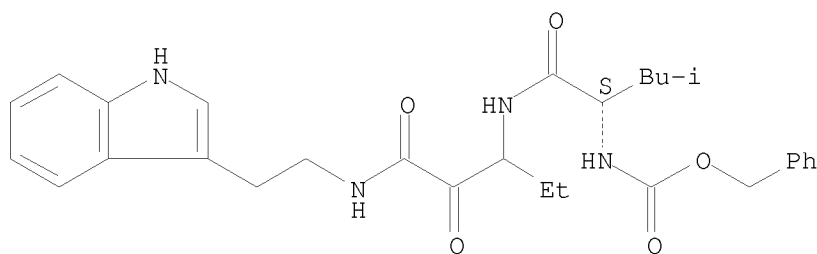
Absolute stereochemistry.



RN 677275-00-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(1H-indol-3-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

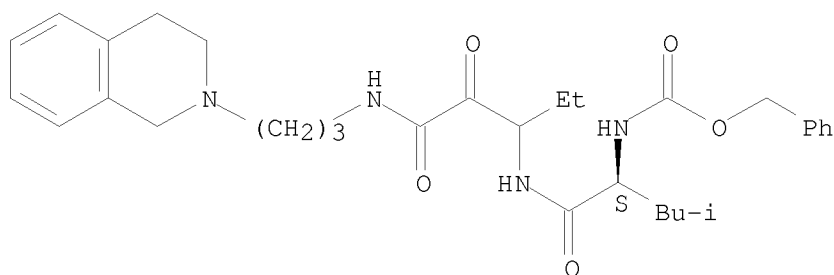
Absolute stereochemistry.



RN 677275-01-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

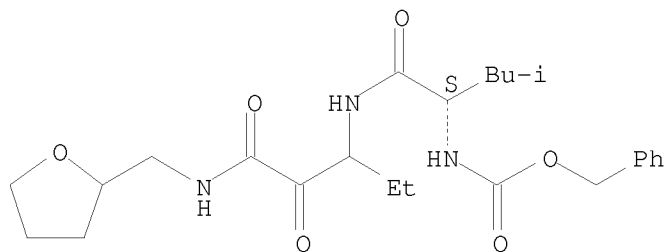
Absolute stereochemistry.



RN 677275-02-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[[tetrahydro-2-furanyl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

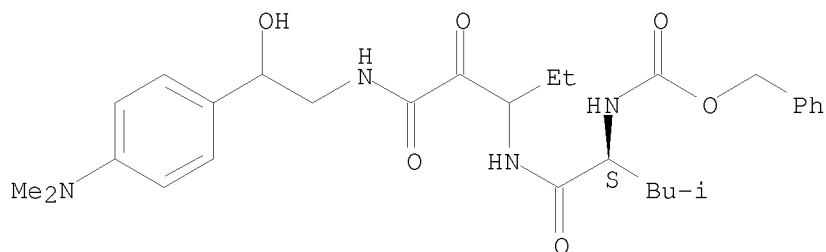
Absolute stereochemistry.



RN 677275-03-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

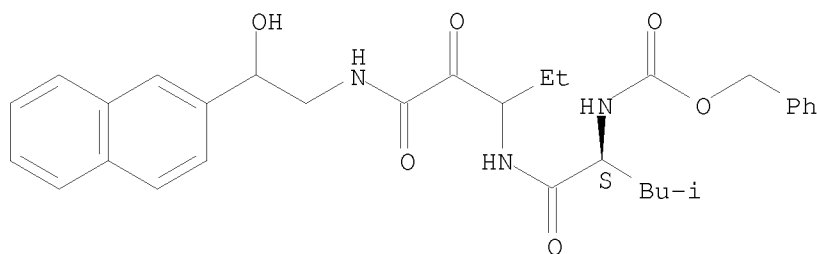
Absolute stereochemistry.



RN 677275-04-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(2-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

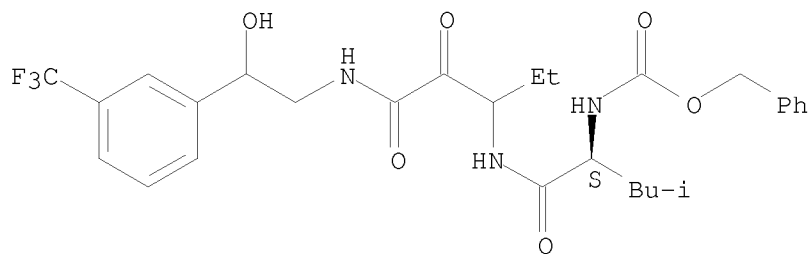
Absolute stereochemistry.



RN 677275-05-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

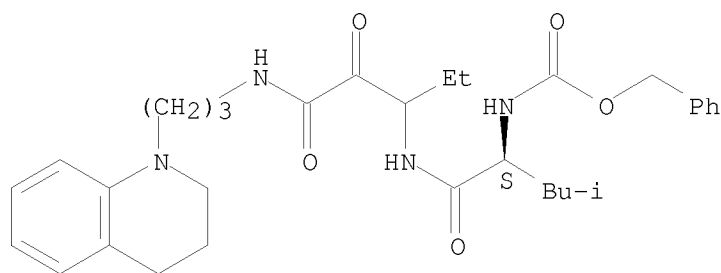
Absolute stereochemistry.



RN 677275-06-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-difluorophenyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

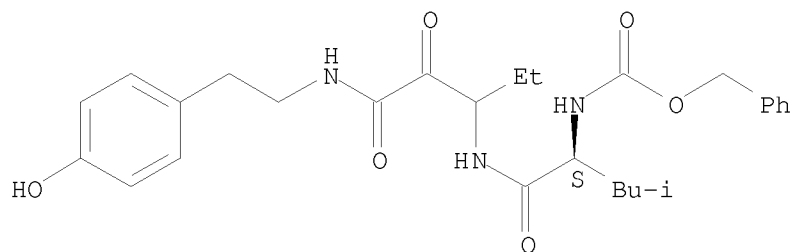
Absolute stereochemistry.



RN 677275-07-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(4-hydroxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

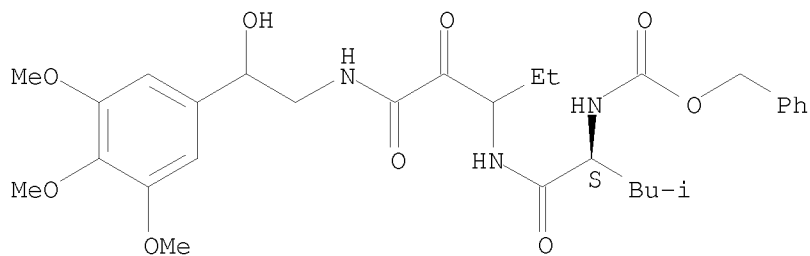
Absolute stereochemistry.



RN 677275-08-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(3,4,5-trimethoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

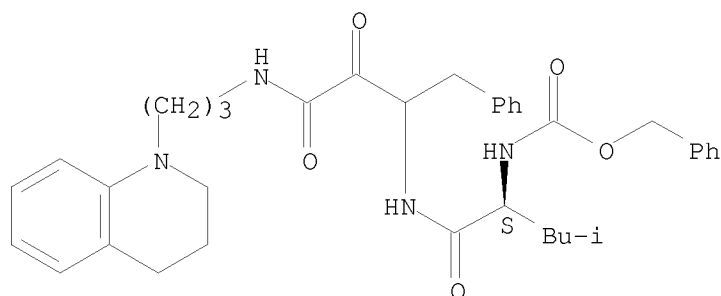
Absolute stereochemistry.



RN 677275-09-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

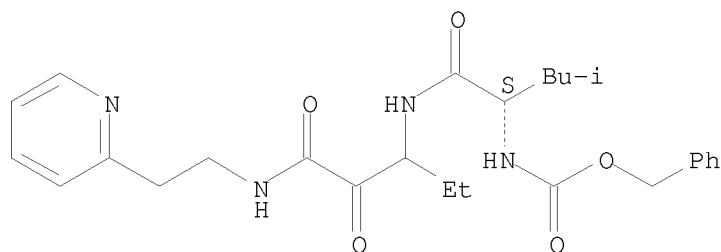
Absolute stereochemistry.



RN 677275-10-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[[2-(2-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

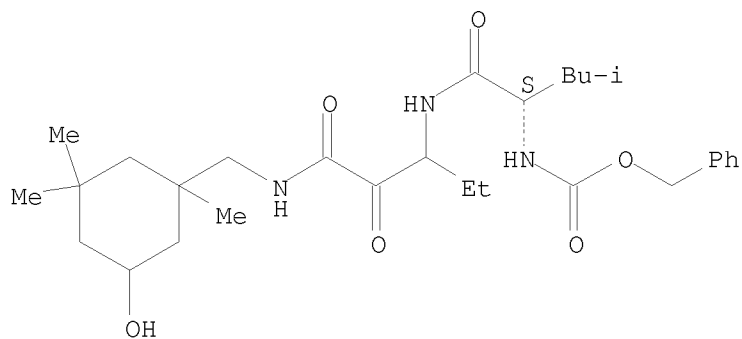


RN 677275-11-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[5-hydroxy-1,3,3-trimethylcyclohexyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

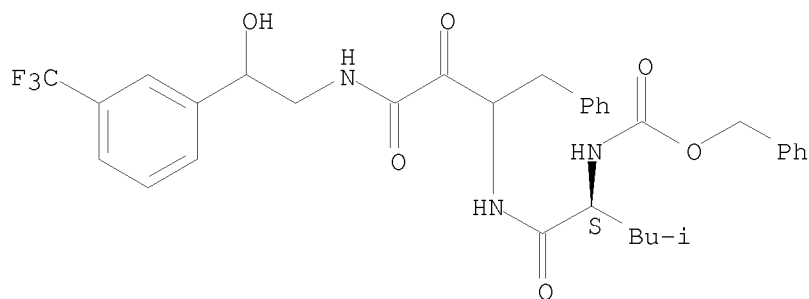




RN 677275-12-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

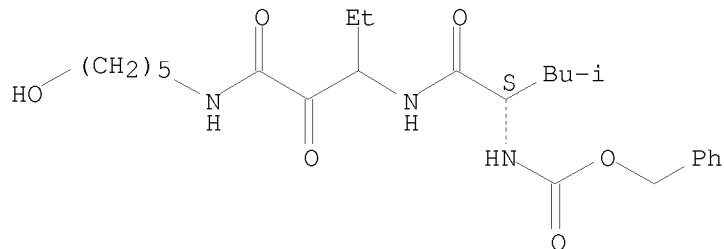
Absolute stereochemistry.



RN 677275-13-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(5-hydroxypentyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

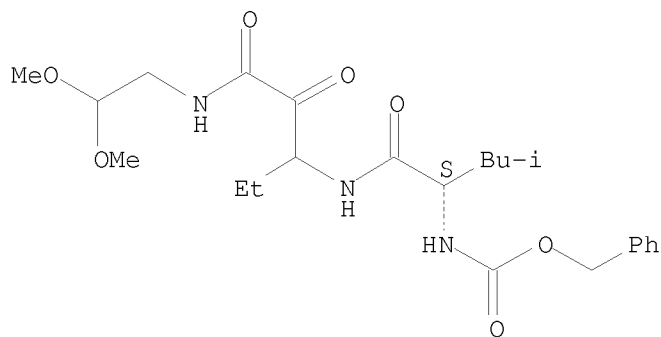
Absolute stereochemistry.



RN 677275-14-8 CAPLUS

CN 12-Oxa-2,5,9-triazatridecanoic acid, 6-ethyl-11-methoxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

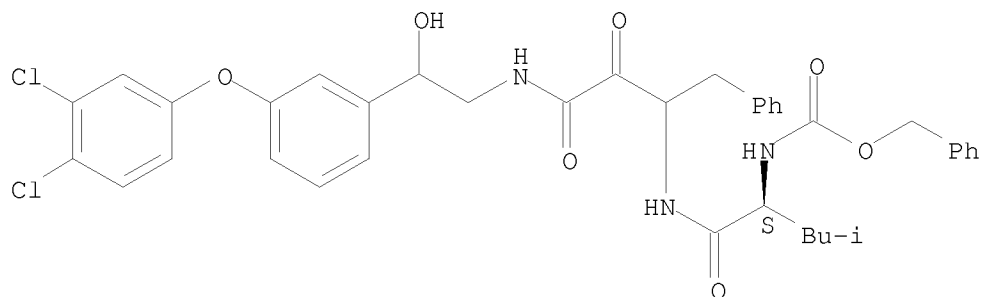
Absolute stereochemistry.



RN 677275-15-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

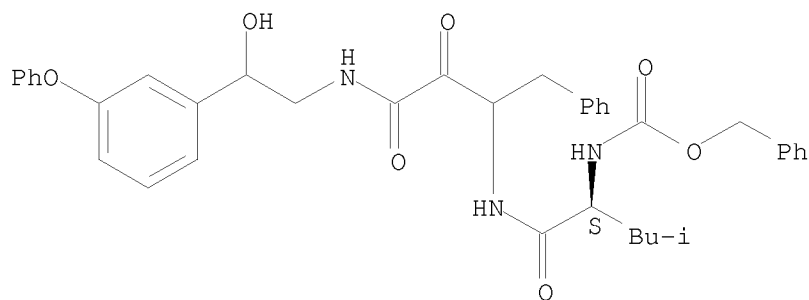
Absolute stereochemistry.



RN 677275-16-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

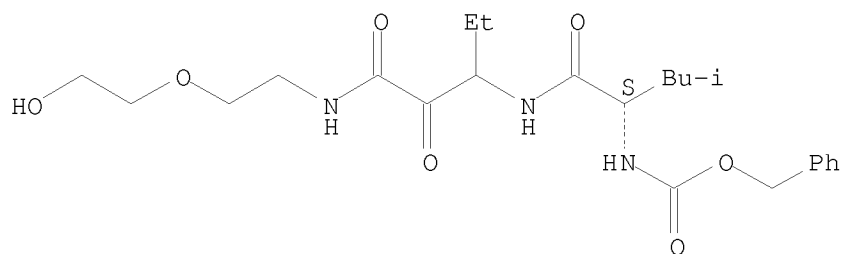
Absolute stereochemistry.



RN 677275-18-2 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid, 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

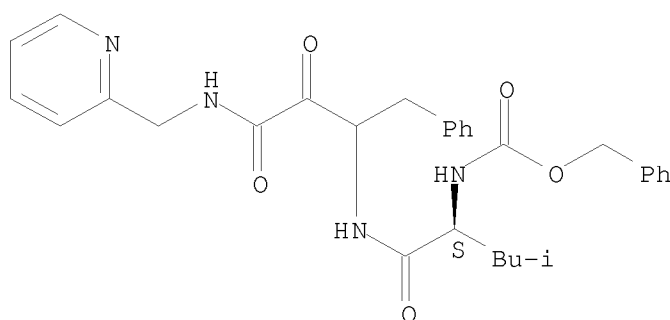
Absolute stereochemistry.



RN 677275-19-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

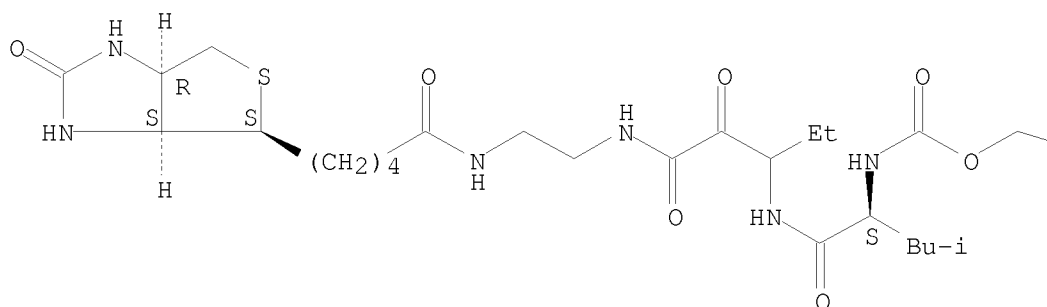


RN 677275-20-6 CAPLUS

CN 2,5,9,12-Tetraazaheptadecanoic acid, 6-ethyl-17-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-3-(2-methylpropyl)-4,7,8,13-tetraoxo-, phenylmethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.

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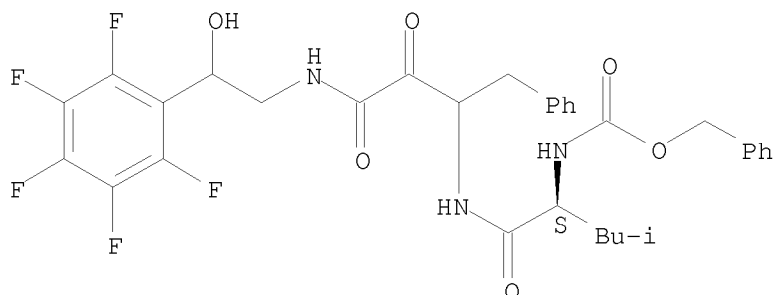


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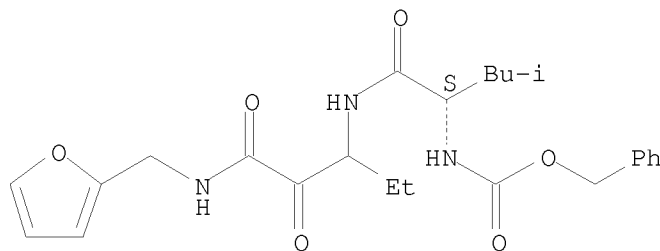
RN 677275-21-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



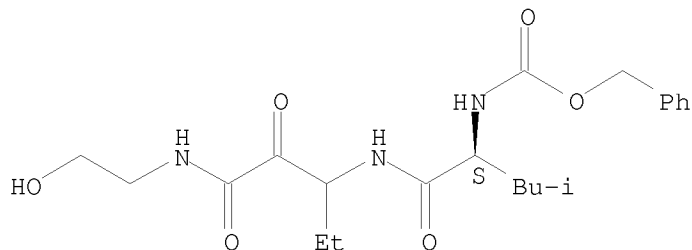
RN 677275-22-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-furanylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



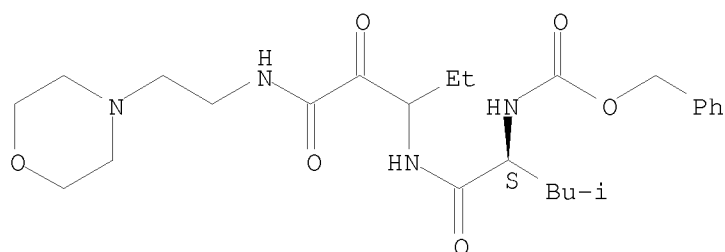
RN 677275-23-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 677275-24-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-(4-morpholinyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

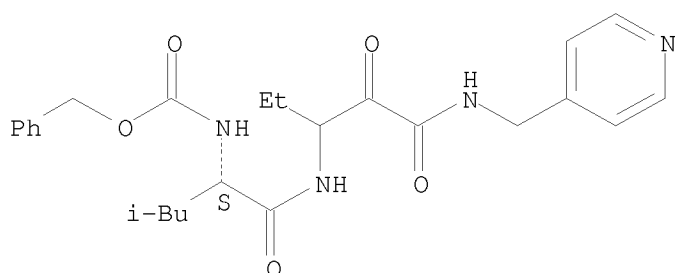
Absolute stereochemistry.



RN 677275-25-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

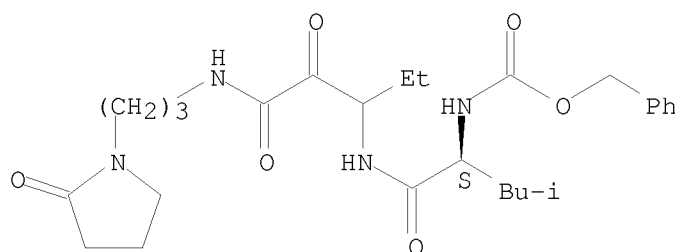
Absolute stereochemistry.



RN 677275-26-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

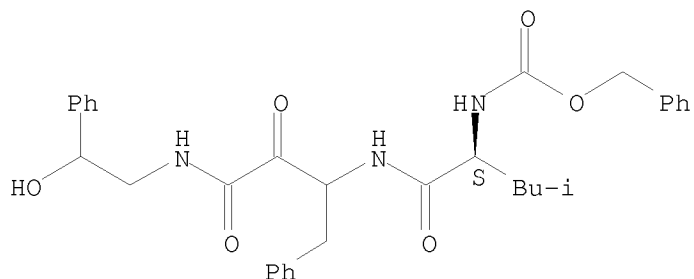
Absolute stereochemistry.



RN 677275-27-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

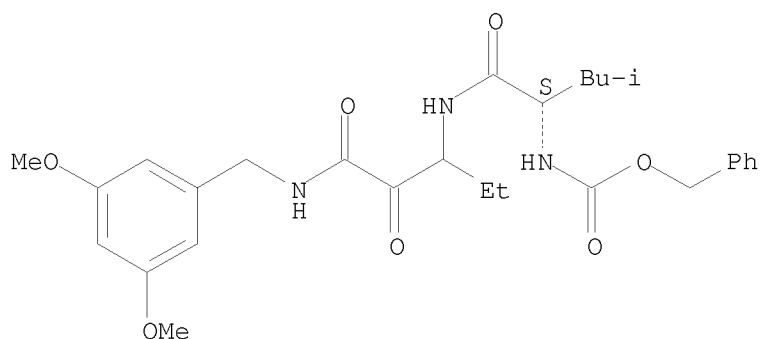
Absolute stereochemistry.



RN 677275-28-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

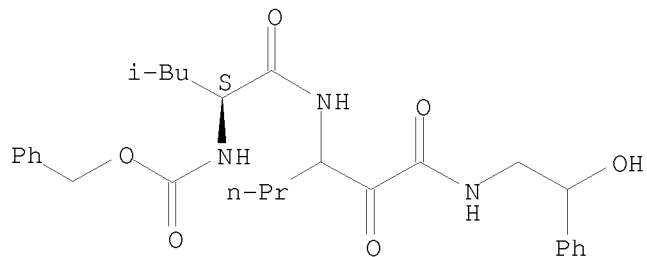
Absolute stereochemistry.



RN 677275-29-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-[(2-hydroxy-2-phenylethyl)amino]oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

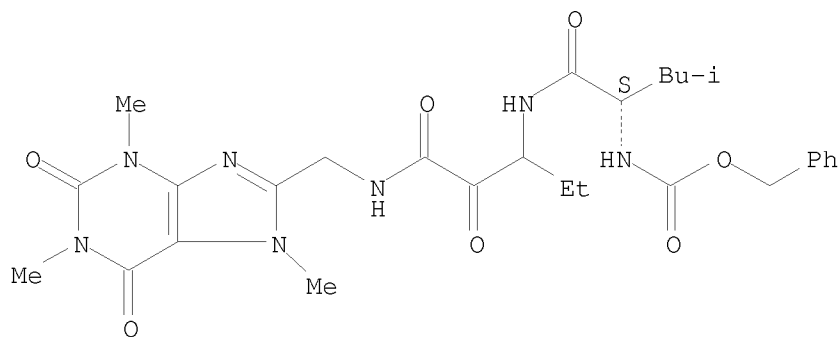
Absolute stereochemistry.



RN 677275-30-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

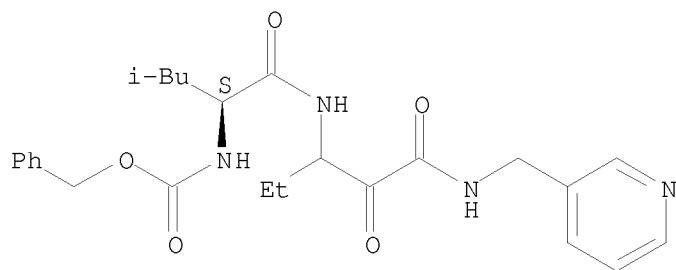
Absolute stereochemistry.



RN 677275-31-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(3-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

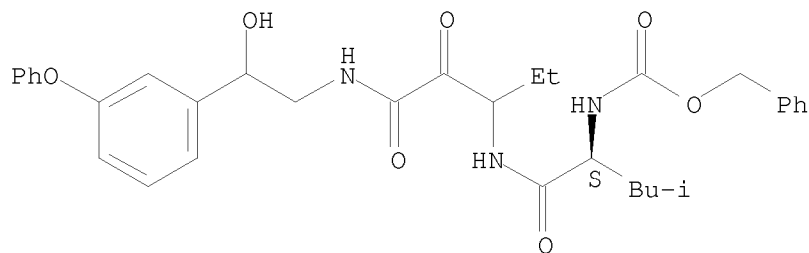
Absolute stereochemistry.



RN 677275-32-0 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (CA INDEX NAME)

Absolute stereochemistry.



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ACCESSION NUMBER: 2003:960457 CAPLUS

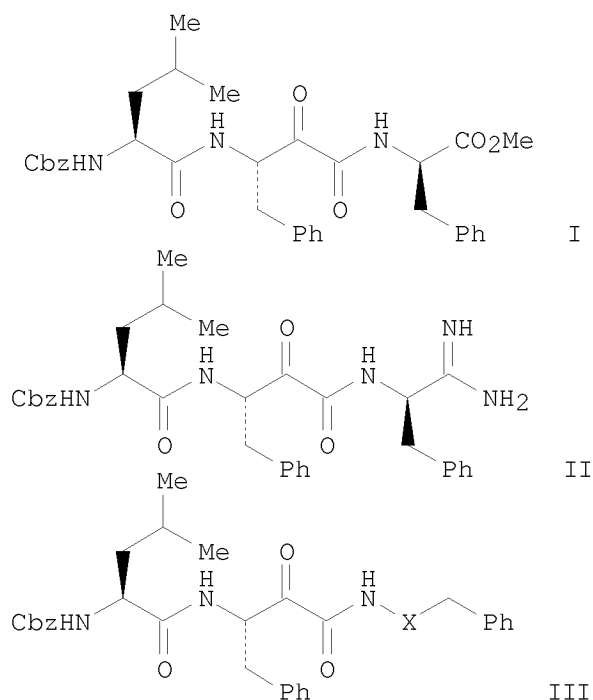
DOCUMENT NUMBER: 140:128677

TITLE: Design, Synthesis, Molecular Modeling Studies, and Calpain Inhibitory Activity of Novel  $\alpha$ -Ketoamides Incorporating Polar Residues at the P1'-Position

AUTHOR(S): Donkor, Isaac O.; Han, Jie; Zheng, Xiaozhang

CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of

Tennessee Health Science Center, Memphis, TN, 38163,  
USA  
SOURCE: Journal of Medicinal Chemistry (2004),  
47(1), 72-79  
CODEN: JMCMAR; ISSN: 0022-2623  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 140:128677  
GI



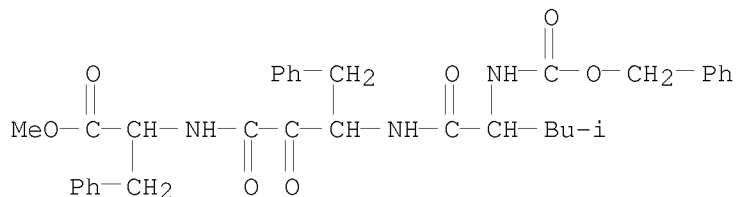
AB A series of novel  $\alpha$ -ketoamides incorporating stereoisomeric residues with different electronic properties at the P1'-position were synthesized to study the electronic requirements for inhibitor binding to the S1'-subsite of calpain I. The results of the study suggested the presence of an acidic amino acid residue at the S1'-subsite of calpain I. For example, ketoamide Me ester Cbz-L-Leu-L-Phe-CO-D-Phe-OMe (I) was over 450-fold more potent than its carboxylic acid derivative Addnl., amidino derivative II was about 6000-fold more potent than the above acid. Furthermore, N-phenethyl amide III (X = CH<sub>2</sub>) was 12-fold less potent than its aza analog III (X = NH). The results are consistent with the presence of an acidic amino acid residue at the S1'-subsite of calpain I. The acidic amino acid residue was found to be Glu261 via mol. modeling studies.

IT 166195-97-7P 649761-74-0P  
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of peptidyl ketoamides as inhibitors of calpain I, and determination of structure-activity relationships from mol. modeling methods)

RN 166195-97-7 CAPLUS



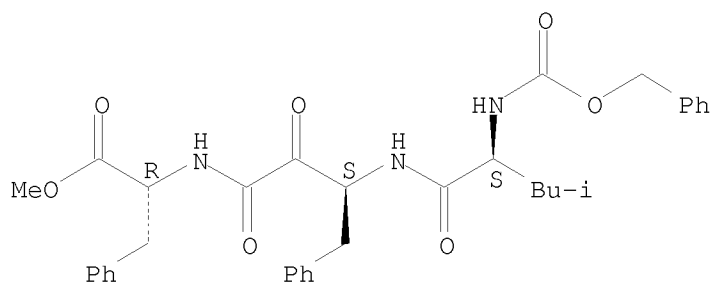
CN L-Phenylalanine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-, methyl ester (9CI) (CA INDEX NAME)



RN 649761-74-0 CAPLUS

CN 2-Oxa-4,7,11-triazatridecan-13-oic acid,  
5-(2-methylpropyl)-3,6,9,10-tetraoxo-1-phenyl-8,12-bis(phenylmethyl)-,  
methyl ester, (5S,8S,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 144231-75-4P 648433-74-3P 648433-76-5P

648433-78-7P 648433-80-1P 648433-83-4P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)

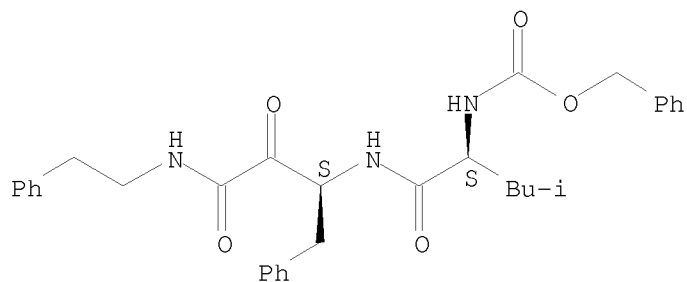
(preparation of peptidyl ketoamides as inhibitors of calpain I, and  
determination of

structure-activity relationships from mol. modeling methods)

RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

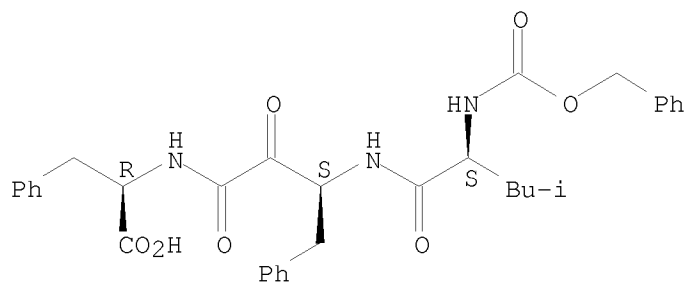
Absolute stereochemistry.



RN 648433-74-3 CAPLUS

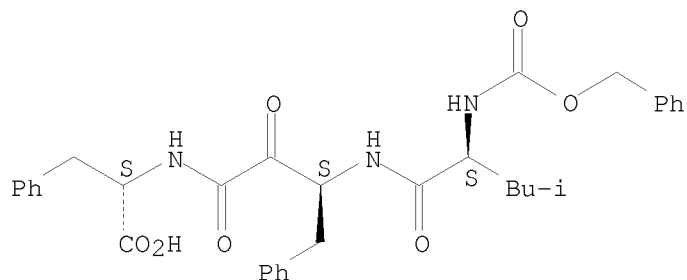
CN 2-Oxa-4,7,11-triazatridecan-13-oic acid,  
5-(2-methylpropyl)-3,6,9,10-tetraoxo-1-phenyl-8,12-bis(phenylmethyl)-,  
(5S,8S,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



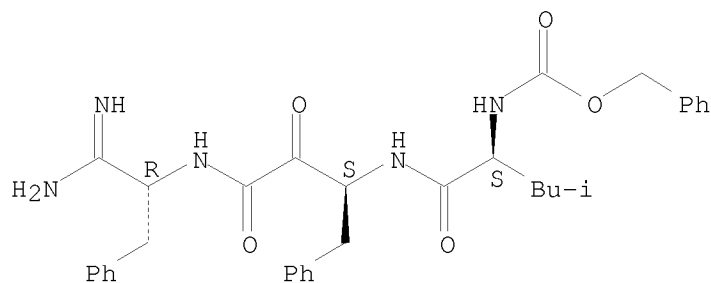
RN 648433-76-5 CAPLUS  
 CN 2-Oxa-4,7,11-triazatridecan-13-oic acid,  
 5-(2-methylpropyl)-3,6,9,10-tetraoxo-1-phenyl-8,12-bis(phenylmethyl)-,  
 (5S,8S,12S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



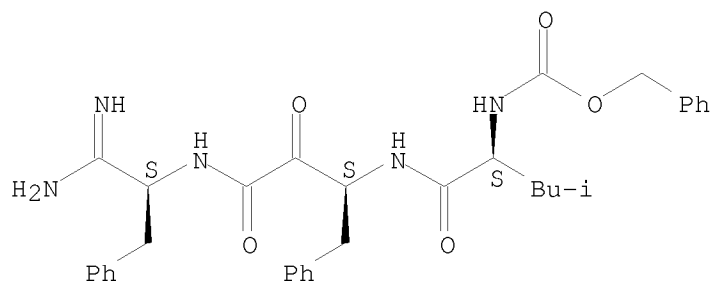
RN 648433-78-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[(1R)-2-amino-2-imino-1-(phenylmethyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



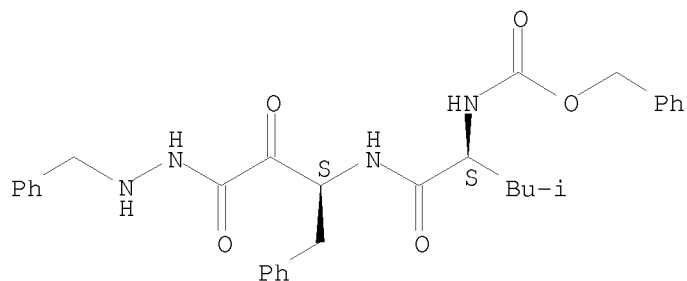
RN 648433-80-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[(1S)-2-amino-2-imino-1-(phenylmethyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



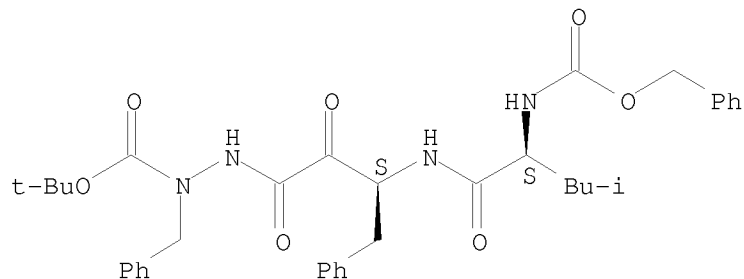
RN 648433-83-4 CAPLUS  
 CN Benzenebutanoic acid,  $\beta$ -[[[(2S)-4-methyl-1-oxo-2-  
 [[(phenylmethoxy)carbonyl]amino]pentyl]amino]- $\alpha$ -oxo-,  
 2-(phenylmethyl)hydrazide, ( $\beta$ S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 648434-03-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of peptidyl ketoamides as inhibitors of calpain I, and  
 determination of  
 structure-activity relationships from mol. modeling methods)  
 RN 648434-03-1 CAPLUS  
 CN 12-Oxa-2,5,9,10-tetraazatetradecanoic acid,  
 13,13-dimethyl-3-(2-methylpropyl)-4,7,8,11-tetraoxo-6,10-bis(phenylmethyl)-  
 , phenylmethyl ester, (3S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:875240 CAPLUS  
 DOCUMENT NUMBER: 139:364944

TITLE: Preparation of diketohydrazine derivatives as cysteine protease inhibitors  
 INVENTOR(S): Hatayama, Akira; Tsuruta, Hiroshi; Ochi, Yasuo; Imawaka, Haruo  
 PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 231 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091202	A1	20031106	WO 2003-JP5252	20030424 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2483998	A1	20031106	CA 2003-2483998	20030424 <--
AU 2003235118	A1	20031110	AU 2003-235118	20030424 <--
EP 1498411	A1	20050119	EP 2003-723188	20030424 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009670	A	20050315	BR 2003-9670	20030424 <--
CN 1649831	A	20050803	CN 2003-809191	20030424 <--
NZ 536728	A	20060728	NZ 2003-536728	20030424 <--
JP 3812678	B2	20060823	JP 2004-501947	20030424 <--
MX 2004PA10523	A	20050608	MX 2004-PA10523	20041022 <--
US 20060111303	A1	20060525	US 2004-512348	20041022 <--
KR 838333	B1	20080613	KR 2004-717135	20041025 <--
ZA 2004009502	A	20050815	ZA 2004-9502	20041124 <--
NO 2004005137	A	20041125	NO 2004-5137	20041125 <--
JP 2006199703	A	20060803	JP 2006-46815	20060223 <--
PRIORITY APPLN. INFO.:			JP 2002-123796	A 20020425 <--
			JP 2004-501947	A3 20030424 <--
			WO 2003-JP5252	W 20030424 <--

OTHER SOURCE(S): MARPAT 139:364944

AB Diketohydrazine (3-amino-2-oxopropanoylhydrazine or 3-aminopropionohydrazide) derivs. represented by the following general formula R-AA1-AA2-NR9CR7R8COCONR10NRYRX [wherein R = H, CycA, halo, (un)substituted C1-8 alkyl, R16CO, R16C(S), R16O2C, R16R17NCO, R16SO2, R16COCH2, R16C(S)CH2; CycA = C3-15 mono-, bi-, or tricyclic carbocyclic ring, 3- to 15-membered mono-, bi-, or tricyclic heterocyclic ring containing 1-4 N, 1 or 2 O and/or 1 or 2 S atom(s); R16 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, CycA; R17, R9 = H, C1-4 alkyl, CycA, CycA-C1-4 alkyl; AA1 = a single bond, (un)substituted NR3CR1R2CO, etc.; R1, R2 = H, (un)substituted C1-8 alkyl, CysA, etc.; R3, R7, R8 = H, C1-8 alkyl, CycA, CycA-C1-8 alkyl, etc.; AA2 = a single bond, NR3CR1R2CO, -CycC-CO-, -NR38-CycD-CO-, etc.; CycC = 3- to 17-membered mono or bicyclic heterocyclic ring; CycD = C3-14 mono or bicyclic carbocyclic ring, 3- to 14-membered mono- or bicyclic heterocyclic ring; R38 = group listed in R17; R10, RY, and RX are not defined] and pharmaceutically acceptable salts thereof are prepared These compds. are inhibitors of cysteine protease, in particular cathepsin K, S, L, B, H, F, Y, or C, calpain, or caspase 1. Because of having a cysteine protease inhibitory activity,

they are useful as remedies for inflammatory diseases, immune diseases, ischemic diseases, respiratory diseases, circulatory diseases, blood diseases, nerve diseases, liver/biliary duct diseases, bone/joint diseases, metabolic diseases, or diseases caused by apoptosis or degradation of bioconstituent proteins. The bone/joint diseases include osteoporosis, chronic articular rheumatism, arthritis, osteoarthritis (arthrosis deformans), hypercalcemia, bone metastasis of carcinoma, or bone fracture. Also disclosed is a bone absorption inhibitor containing the above compound. Because of having an elastase inhibitory activity, these compds. are also useful as remedies for COPD (chronic obstructive pulmonary disease) and so on. N'-(3-tert-butyl-1,3-thiazolidin-2-ylidene)-3-cyclohexylcarbonylamino-2-oxo-3-(tetrahydropyran-4-yl)propionohydrazide hydrochloride inhibited cathepsin K with  $K_i$  of 2.5 nM. A tablet and an ampule containing N'-(3-methyl-1,3-thiazolidin-2-ylidene)-(3S)-3-cyclohexylcarbonylamino-2-oxo-5-methylhexanohydrazide hydrochloride were described.

IT 620612-98-8P 620613-01-6P 620613-02-7P  
620614-12-2P 620614-16-6P 620614-17-7P  
620614-19-9P

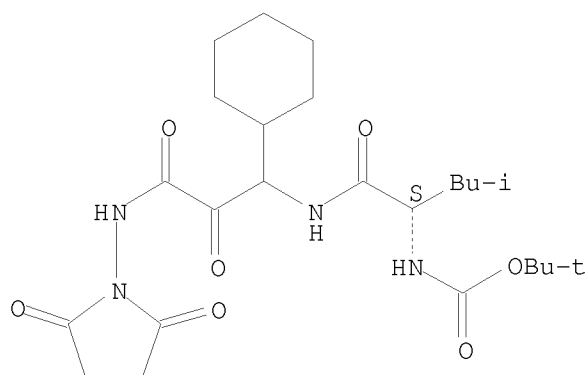
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diketohydrazine derivs. as cysteine protease inhibitors and therapeutic agents)

RN 620612-98-8 CAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-3-cyclohexyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo- (9CI) (CA INDEX NAME)

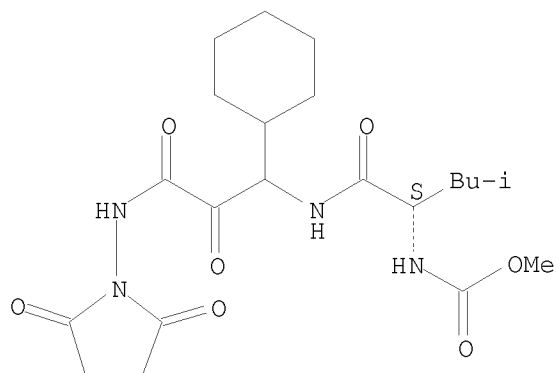
Absolute stereochemistry.



RN 620613-01-6 CAPLUS

CN  $\beta$ -Alaninamide, N-(methoxycarbonyl)-L-leucyl-3-cyclohexyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo- (9CI) (CA INDEX NAME)

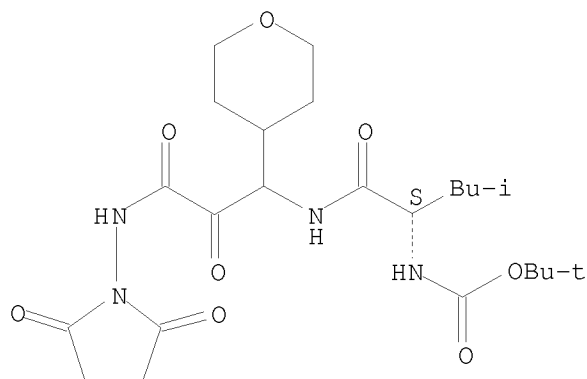
Absolute stereochemistry.



RN 620613-02-7 CAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo-3-(tetrahydro-2H-pyran-4-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

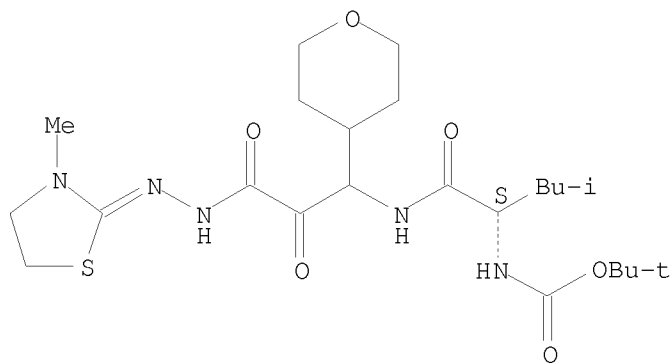


RN 620614-12-2 CAPLUS

CN 2H-Pyran-4-propanoic acid,  $\beta$ -[[ (2S)-2-[[ (1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]tetrahydro- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

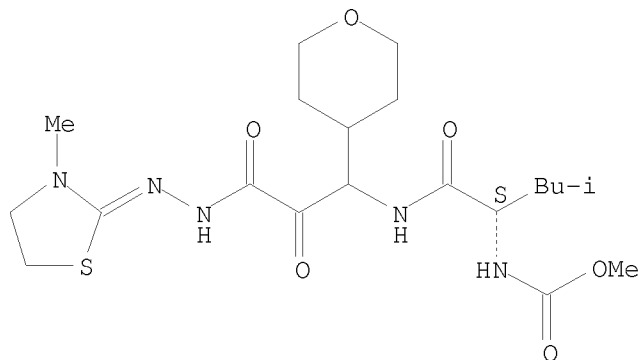


RN 620614-16-6 CAPLUS

CN 2H-Pyran-4-propanoic acid, tetrahydro- $\beta$ -[[ (2S)-2-

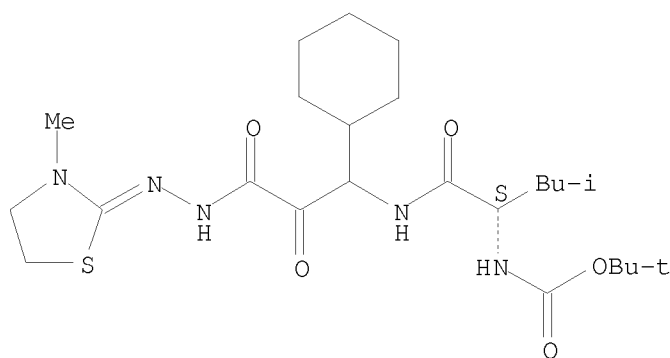
[(methoxycarbonyl)amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-,  
2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



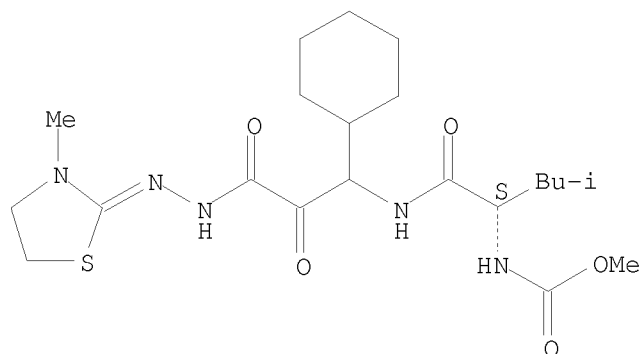
RN 620614-17-7 CAPLUS  
CN Cyclohexanepropanoic acid,  $\beta$ -[[[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



RN 620614-19-9 CAPLUS  
CN Cyclohexanepropanoic acid,  $\beta$ -[[[(2S)-2-[(methoxycarbonyl)amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:814551 CAPLUS

DOCUMENT NUMBER: 140:175070

TITLE: Cellular Events Preceding Acetaminophen  
Cataractogenesis Studied by Confocal Fluorescence  
Microscopy

AUTHOR(S): Mathur, Priya; Peshenko, Igor V.; Shichi, Hitoshi

CORPORATE SOURCE: Department of Ophthalmology, Wayne State, University  
School of Medicine, Detroit, MI, USA

SOURCE: Journal of Ocular Pharmacology and Therapeutics (2003), 19(5), 483-492

CODEN: JOPTFU; ISSN: 1080-7683

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Acetaminophen (APAP) is biotransformed by hepatic cytochrome P 450 (CYP) enzymes to the cataractogenic metabolite N-acetyl-p-benzoquinone imine (NAPQI). In the previous studies in which NAPQI was injected into the anterior chamber of mouse eye, we observed mitochondrial dysfunction and disturbances in Ca<sup>2+</sup> homeostasis in the lens epithelium, and activation of the non-lysosomal neutral protease calpain. In this work we investigated whether i.p. injection of APAP elicits similar cellular responses in the lens epithelium prior to the onset of lens opacity development. Following APAP injection, reactive oxygen species generation, intracellular free Ca<sup>2+</sup> increase and calpain activation in the lens epithelium were determined in situ by fluorescence confocal microscopy. It was found that cellular events in the lens prior to the onset of opacification were essentially identical to those elicited by NAPQI. In addition, lens calpain activities were characterized based on their Ca<sup>2+</sup> requirement and several calpain inhibitors were shown to prevent cataract development.

IT 160399-35-9, AK 295

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cellular events preceding acetaminophen cataractogenesis studied by confocal fluorescence microscopy)

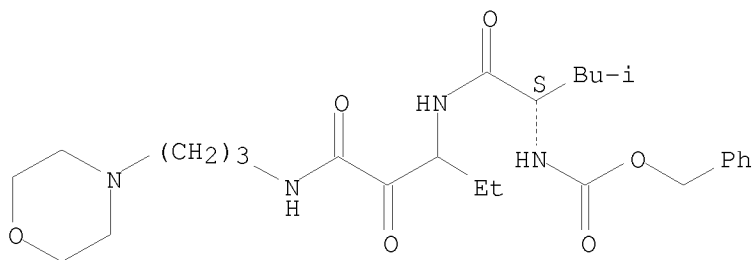
RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Currently available stereo shown.





REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:633330 CAPLUS

DOCUMENT NUMBER: 139:164974

TITLE: Epoxycarboxylic acid amides, azides and amino alcohols and processes for preparation of  $\alpha$ -keto amides by using them

INVENTOR(S): Kobayashi, Nobuo; Koji, Tsuneo; Fujita, Takashi; Nishimura, Tomofumi; Hosoda, Akihiko

PATENT ASSIGNEE(S): Seikagaku Corporation, Japan

SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of Appl. No. PCT/JP01/05668.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

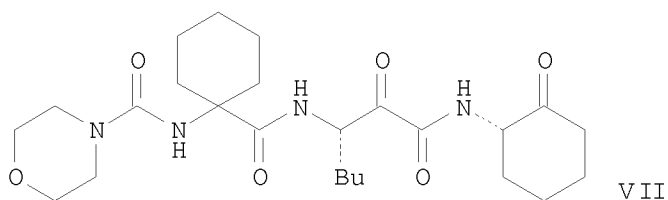
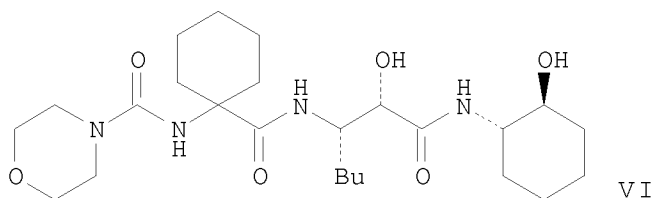
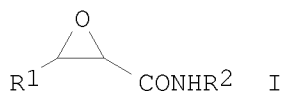
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030153788	A1	20030814	US 2002-331702	20021230 <--
US 7326799	B2	20080205		
JP 2002080438	A	20020319	JP 2001-172689	20010607 <--
JP 2002080441	A	20020319	JP 2001-172751	20010607 <--
JP 2002179664	A	20020626	JP 2001-172711	20010607 <--
WO 2002002546	A1	20020110	WO 2001-JP5668	20010629 <--
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20080058516	A1	20080306	US 2007-980056	20071030 <--
US 20080064873	A1	20080313	US 2007-981120	20071031 <--
PRIORITY APPLN. INFO.:				
			JP 2000-198089	A 20000630 <--
			JP 2000-198090	A 20000630 <--
			JP 2000-198091	A 20000630 <--
			WO 2001-JP5668	A2 20010629 <--
			US 2002-331702	A3 20021230 <--

OTHER SOURCE(S): CASREACT 139:164974; MARPAT 139:164974

GI



AB    Epoxycarboxylic acid amides I [R1, R2 = (un)substituted linear, branched, or cyclic alkyl or alkenyl, (un)substituted aromatic hydrocarbyl or heterocyclyl], azides R1CHN3CH(OH)CONHR2 (II; R1, R2 = same as above), and amino alcs. ( $\alpha$ -hydroxy amides) R3CO-X-CR4R5CONHCHR1CH(OH)CONHR2 [III; R1, R2 = same as above; R3 = any group given for R1/R2, R6O or R7NR8 [R6-R8 = any group given for R1/R2; R7, R8 may also be H]; X = O, NR9 [R9 = H, (un)substituted linear, branched, or cyclic alkyl]; R4, R5 = any group given for R1/R2 or may form a ring with each other or with X] were prepared. Oxidation of the amino alc. III gives  $\alpha$ -keto amide compds. R3CO-X-CR4R5CONHCHR1COCONHR2 (IV; R1-R5, X = same as above). The invention provides intermediates I, II, and III from which  $\alpha$ -keto amide compds. IV having protease inhibiting activity (no data) can be prepared extremely economically and stereoselectively. Thus, a THF solution of 2.3 g (2S,3R)-3-butyloxirane-2-carboxylic acid dicyclohexylamine salt (preparation given) was treated with a THF solution of 844 mg pivaloyl chloride under ice-cooling, stirred at the same temperature for 15 min and then at room temperature, filtered to remove insol. matter, treated with a THF solution of

806

mg (1S,2S)-2-aminocyclohexanol, and stirred at room temperature for 2 h to give 100% (2S,3R)-N-[(1S,2S)-2-hydroxycyclohexan-1-yl]-3-butyloxirane-2-carboxamide. A suspension of the latter compound (1.64 g), 910 mg NaN3, and 868 mg anhydrous MgSO4 in 30 mL was refluxed for 5 h to give 73% (2S,3S)-N-[(1S,2S)-2-hydroxycyclohexan-1-yl]-3-azido-2-hydroxyheptanamide which (1.45 g) was hydrogenated over 5% Pd-C in 30 MeOH under hydrogen atmospheric for 18 h to give 91%

(2S,3S)-N-[(1S,2S)-2-hydroxycyclohexan-1-yl]-3-amino-2-hydroxyheptanamide (V). A THF solution of 256 mg 1-[N-(morpholin-4-ylcarbonyl)amino]cyclohexanecarboxylic acid and 202 mg Et3N was treated with a THF solution of 121 mg pivaloyl chloride under ice-cooling, stirred at the same temperature for 2 h and then at room

temperature for

18 h and filtered to remove insol. matter, treated with a CHCl3 solution of 258 mg V, and stirred for 3 h to give an amino alc. (VI) in 94% yield. VI was oxidized by SO3-pyridine complex/DMSO in the presence of N,N-diisopropylethylamine in CH2Cl2 at 0° for 3 h to give an  $\alpha$ -keto amide (VII) in 87% yield.

IT    387400-79-5P, (2S)-N-[(3S)-1,2-Dioxo-1-[N-[(1S)-2-oxocyclohexan-1-

yl]amino]heptan-3-yl]-4-methyl-2-[N-(phenylmethoxycarbonyl)amino]pentanamide

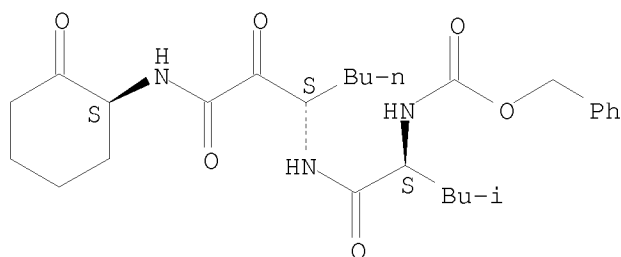
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(stereoselective preparation of epoxycarboxylic acid amides, azides, and amino alcs. as intermediates for protease-inhibitory  $\alpha$ -keto amides)

RN 387400-79-5 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-1-[oxo[(1S)-2-oxocyclohexyl]amino]acetyl]pentyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:777693 CAPLUS

DOCUMENT NUMBER: 137:299911

TITLE: Neuroprotectant formulations

INVENTOR(S): Hesson, David P.; Frazer, Glenn D.; Ross, Douglas

PATENT ASSIGNEE(S): Neuron Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078670	A1	20021010	WO 2002-US5885	20020228 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002305940	A1	20021015	AU 2002-305940	20020228 <--
EP 1370240	A1	20031217	EP 2002-733809	20020228 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 20020193285	A1	20021219	US 2002-90441	20020304 <--
PRIORITY APPLN. INFO.:			US 2001-331360P	P 20010302 <--
			US 2001-798880	A 20010302 <--
			WO 2002-US5885	W 20020228 <--

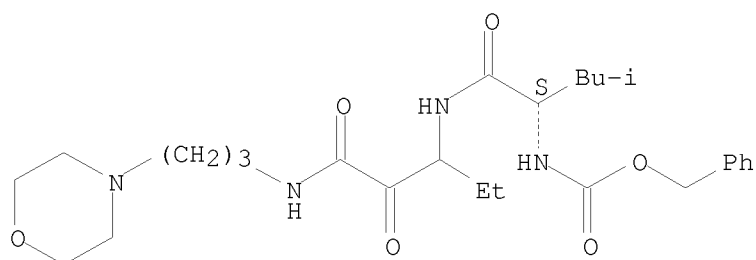
AB A method of treating an animal that has suffered damage to cerebrospinal tissue or that has an indication creating a risk of damage to cerebrospinal tissue, comprises injecting a physiol. acceptable cerebrospinal perfusion fluid into a first catheter into the cerebrospinal pathway. The cerebrospinal perfusion fluid has a neuroprotecting effective amount of a neuroprotectant, withdrawing fluid at a second catheter into the cerebrospinal pathway to create a flow and flow pathway between the first and second catheters and c. maintaining the flow for a period of time adapted to perfuse an affected tissue.

IT 160399-35-9, AK 295  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (neuroprotectant formulations)

RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Currently available stereo shown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:465963 CAPLUS

DOCUMENT NUMBER: 137:47443

TITLE: Preparation of peptides and compositions containing them for treatment of parasitic infections

INVENTOR(S): Lim-Wilby, Marguerita; Semple, Joseph Edward; Araldi, Gian L.; Goldman, Erick A.; Weinhouse, Michael I.

PATENT ASSIGNEE(S): Corvas International, Inc., USA

SOURCE: PCT Int. Appl., 112 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002048097	A1	20020620	WO 2001-US48032	20011211 <--
WO 2002048097	A9	20030508		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,

GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 AU 2002032558 A 20020624 AU 2002-32558 20011211 <--  
 US 20020107266 A1 20020808 US 2001-14171 20011211 <--  
 PRIORITY APPLN. INFO.: US 2000-255221P P 20001212 <--  
 WO 2001-US48032 W 20011211 <--

OTHER SOURCE(S): MARPAT 137:47443

AB Comps. W-X-D(H)-CHR2CONH-E(H)(R1)-Y-Z [W, R1, R2 = H, alkyl, alkenyl, alkynyl, oxaalkyl, cycloalkyl, aryl, heteroaryl, etc.; X = a direct link, CO, O2C, SOn (n = 0-2); D = nitrogen; E = carbon; Y = CO, A'(H):CHCO, or A'(O)CONH (A' = carbon); Z = G, J, or L (G = H, J and L are each H, alkyl, alkenyl, alkynyl, oxaalkyl, etc.) (with provisos)] and pharmaceutical compns. were prepared for use as anti-parasitic agents, particularly in the treatment, prevention or amelioration of one or more symptoms of malaria or Chagas' disease. Methods are provided for modulating the activity of falcipain or cruzain, preferably inhibiting falcipain or cruzain, with the compds. and compns. of the invention. Thus, Me (E)-4-[N-(benzyloxycarbonyl)phenylalaninyl]amino]-6-phenyl-2-hexenoate was prepared in 3 steps starting from (S)-2-[N-(tert-butoxycarbonyl)amino]-4-phenylbutanoic acid. In assays for inhibition of falcipain or cruzain, almost all of the compds. of the invention have an IC50 < 100 nM, many of the compds. have an IC50 .ltorsim. 50 nM, and some of the compds. have an IC50 .ltorsim. 10 nM.

IT 438045-23-9P 438045-26-2P 438045-28-4P  
 438045-32-0P

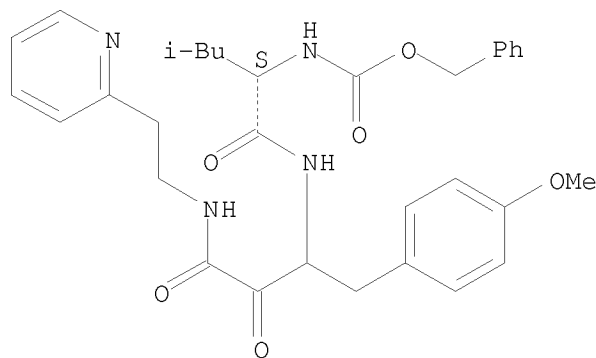
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides and compns. containing them for treatment of parasitic infections)

RN 438045-23-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-[(4-methoxyphenyl)methyl]-2,3-dioxo-3-[[2-(2-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

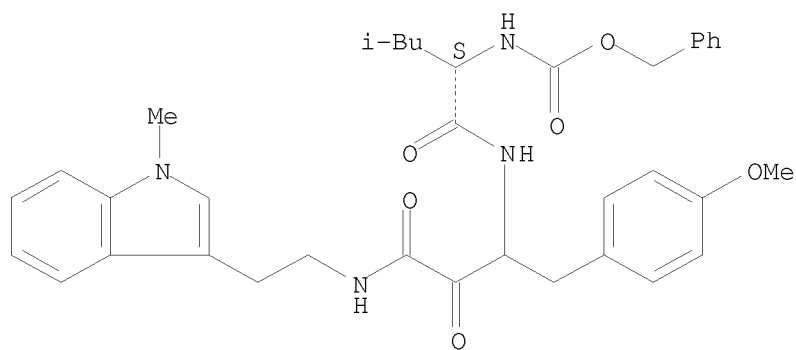
Absolute stereochemistry.



RN 438045-26-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-[(4-methoxyphenyl)methyl]-3-[[2-(1-methyl-1H-indol-3-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

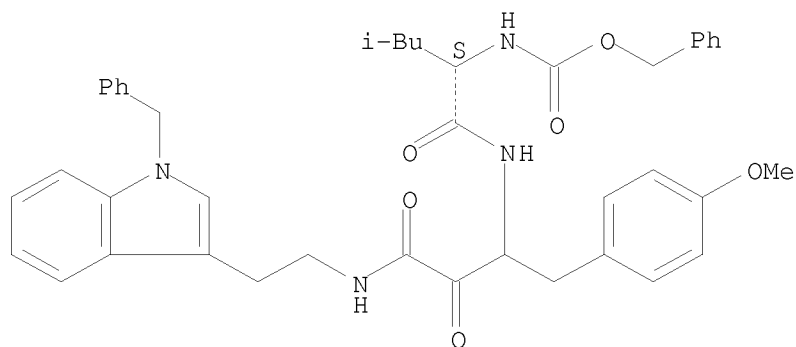
Absolute stereochemistry.



RN 438045-28-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-[(4-methoxyphenyl)methyl]-2,3-dioxo-3-[[2-[1-(phenylmethyl)-1H-indol-3-yl]ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

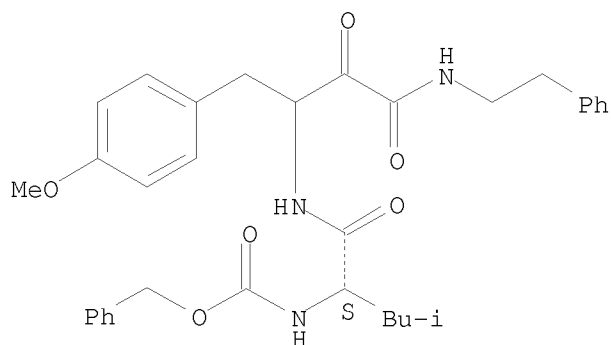
Absolute stereochemistry.



RN 438045-32-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-[(4-methoxyphenyl)methyl]-2,3-dioxo-3-[[2-(phenylethyl)amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:214354 CAPLUS

DOCUMENT NUMBER: 137:103795  
 TITLE: Peptidyl  $\alpha$ -keto amide inhibitor of calpain blocks excitotoxic damage without affecting signal transduction events  
 AUTHOR(S): Caba, Ebru; Brown, Queenie B.; Kawasaki, Brian; Bahr, Ben A.  
 CORPORATE SOURCE: Department of Pharmaceutical Sciences and the Neurosciences Program, University of Connecticut, Storrs, CT, 06269-2092, USA  
 SOURCE: Journal of Neuroscience Research (2002), 67(6), 787-794  
 CODEN: JNREDK; ISSN: 0360-4012  
 PUBLISHER: Wiley-Liss, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

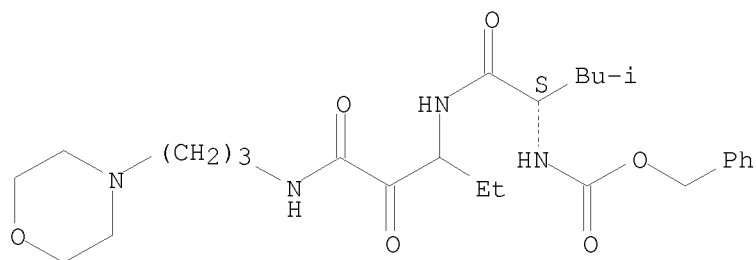
AB The cysteine protease calpain is activated by calcium and has a wide range of substrates. Calpain-mediated cellular damage is associated with many neuropathologies, and calpain also plays a role in signal transduction events that are essential for cell maintenance, including the activation of important kinases and transcription factors. In the present study, the hippocampal slice culture was used as a model of excitotoxicity to test whether the neuroprotection elicited by selective calpain inhibition is associated with changes in cell signaling. Peptidyl  $\alpha$ -keto amide and  $\alpha$ -keto acid inhibitors reduced both calpain-mediated cytoskeletal damage and the concomitant synaptic deterioration resulting from an N-methyl-D-aspartate exposure. The  $\alpha$ -keto amide CX295 was protective when infused into slice cultures before or after the excitotoxic episode. The slices protected with CX295 exhibited normal activation levels of mitogen-activated protein kinase and the transcription factor nuclear factor- $\kappa$ B. Thus, selective inhibition of calpain provides neuroprotection without influencing critical signaling pathways.

IT 160399-35-9, CX 295  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (peptidyl  $\alpha$ -keto amide inhibitor (CX295) of calpain blocks excitotoxic damage without affecting signal transduction events)

RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Currently available stereo shown.

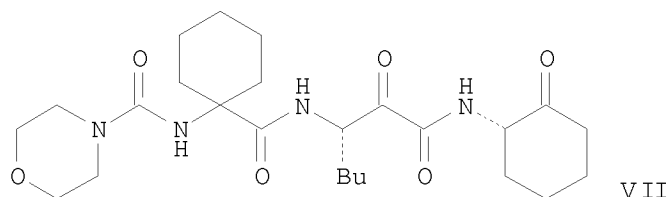
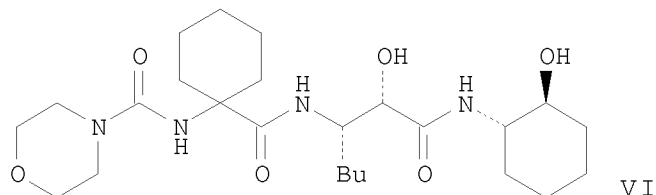


REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2002:31435 CAPLUS  
 DOCUMENT NUMBER: 136:86053

TITLE: Epoxycarboxylic acid amides, azides and amino alcohols and processes for preparation of  $\alpha$ -keto amides by using them  
 INVENTOR(S): Kobayashi, Nobuo; Koji, Tsuneo; Fujita, Takashi; Nishimura, Tomofumi; Hosoda, Akihiko  
 PATENT ASSIGNEE(S): Seikagaku Corporation, Japan  
 SOURCE: PCT Int. Appl., 71 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002546	A1	20020110	WO 2001-JP5668	20010629 <--
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2002080438	A	20020319	JP 2001-172689	20010607 <--
JP 2002080441	A	20020319	JP 2001-172751	20010607 <--
JP 2002179664	A	20020626	JP 2001-172711	20010607 <--
CA 2414960	A1	20020110	CA 2001-2414960	20010629 <--
AU 2001067886	A	20020114	AU 2001-67886	20010629 <--
EP 1295876	A1	20030326	EP 2001-945730	20010629 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 20030153788	A1	20030814	US 2002-331702	20021230 <--
US 7326799	B2	20080205		
US 20080058516	A1	20080306	US 2007-980056	20071030 <--
US 20080064873	A1	20080313	US 2007-981120	20071031 <--
PRIORITY APPLN. INFO.:				
			JP 2000-198089	A 20000630 <--
			JP 2000-198090	A 20000630 <--
			JP 2000-198091	A 20000630 <--
			WO 2001-JP5668	W 20010629 <--
			US 2002-331702	A3 20021230 <--
OTHER SOURCE(S): CASREACT 136:86053; MARPAT 136:86053				
GI				





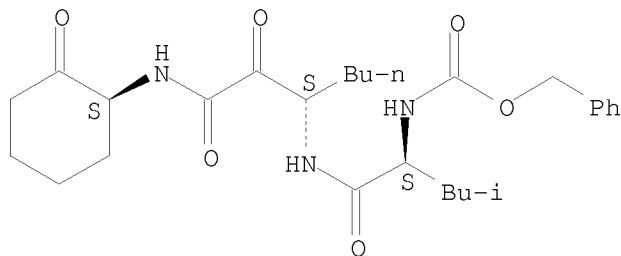
AB Epoxycarboxylic acid amides [I; R1, R2 = (un)substituted linear, branched, or cyclic alkyl or alkenyl, (un)substituted aromatic hydrocarbyl or heterocyclyl], azides represented by the general formula  $R1CHN3CH(OH)CONHR2$  (II; R1, R2 = same as above), and amino alcs. ( $\alpha$ -hydroxy amides) represented by the general formula  $R3CO-X-CR4R5CONHCHR1CH(OH)CONHR2$  [III; R1, R2 = same as above; R3 = (un)substituted linear, branched, or cyclic alkyl or alkenyl, (un)substituted aromatic hydrocarbyl or heterocyclyl, R6O, R7NR8 (wherein R6 = (un)substituted linear, branched, or cyclic alkyl or alkenyl, (un)substituted aromatic hydrocarbyl or heterocyclyl; R7, R8 = H, (un)substituted linear, branched, or cyclic alkyl or alkenyl, (un)substituted aromatic hydrocarbyl or heterocyclyl); X = O, NR9 (wherein H, (un)substituted linear, branched, or cyclic alkyl); or R4 and R5 are taken together to form a ring.] are prepared. Oxidation of the amino alc. III gives  $\alpha$ -keto amide compds. represented by general formula  $R3CO-X-CR4R5CONHCHR1COCONHR2$  (IV; R1 - R5, X = same as above). The invention provides intermediates I, II, and III from which  $\alpha$ -keto amide compds. IV having protease inhibiting activity (no data) can be prepared extremely economically and stereoselectively. Thus, a THF solution of 2.3 g (2S,3R)-3-butyloxirane-2-carboxylic acid dicyclohexylamine salt (preparation given) was treated with a THF solution of 844 mg pivaloyl chloride under ice-cooling, stirred at the same temperature for 15 min and then at room temperature, filtered to remove insol. matter, treated with a THF solution of 806 mg (1S,2S)-2-aminocyclohexanol, and stirred at room temperature for 2 h to give 100% (2S,3R)-N-[(1S,2S)-2-hydroxycyclohexan-1-yl]-3-butyloxirane-2-carboxamide. A suspension of the latter compound (1.64 g), 910 mg NaN<sub>3</sub>, and 868 mg anhydrous MgSO<sub>4</sub> in 30 mL was refluxed for 5 h to give 73% (2S,3S)-N-[(1S,2S)-2-hydroxycyclohexan-1-yl]-3-azido-2-hydroxyheptanamide which (1.45 g) was hydrogenated over 5% Pd-C in 30 MeOH under hydrogen atmospheric for 18 h to give 91% (2S,3S)-N-[(1S,2S)-2-hydroxycyclohexan-1-yl]-3-amino-2-hydroxyheptanamide (V). A THF solution of 256 mg 1-[N-(morpholin-4-ylcarbonyl)amino]cyclohexanecarboxylic acid and 202 mg Et<sub>3</sub>N was treated with a THF solution of 121 mg pivaloyl chloride under ice-cooling, stirred at the same temperature for 2 h and then at room temperature for 18 h and filtered to remove insol. matter, treated with a CHCl<sub>3</sub> solution of 258 mg V, and stirred for 3 h to give an amino alc. (VI) in 94% yield. VI was oxidized by SO<sub>3</sub>-pyridine complex/DMSO in the presence of N,N-diisopropylethylamine in CH<sub>2</sub>Cl<sub>2</sub> at 0° for 3 h to give an  $\alpha$ -keto amide (VII) in 87% yield.

IT 387400-79-5P, (2S)-N-[(3S)-1,2-Dioxo-1-[N-[(1S)-2-oxocyclohexan-1-yl]amino]heptan-3-yl]-4-methyl-2-[N-(phenylmethoxycarbonyl)amino]pentanamide  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (stereoselective preparation of epoxycarboxylic acid amides, azides, and amino alcs. as intermediates for protease-inhibitory  $\alpha$ -keto amides)

RN 387400-79-5 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-1-[oxo[(1S)-2-oxocyclohexyl]amino]acetyl]pentyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:674637 CAPLUS

DOCUMENT NUMBER: 136:48333

TITLE: Potent peptide  $\alpha$ -Ketohydroxamate inhibitors of recombinant human calpain I

AUTHOR(S): Josef, K. A.; Kauer, F. W.; Bihovsky, R.

CORPORATE SOURCE: Cephalon, Inc., West Chester, PA, 19380-4245, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(19), 2615-2617

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:48333

AB A series of potent dipeptide and tripeptide  $\alpha$ -ketohydroxamic esters was prepared as inhibitors of recombinant human calpain I. Compound 3c, a Cbz-Leu-Phe hydroxamate, displayed the greatest potency against calpain I ( $IC_{50}=6$  nM), while two compds., 3l and 3m, both possessing the Cbz-Leu-Leu-Phe sequence, were the most potent ( $IC_{50}=0.2$   $\mu$ M) in a MOLT-4 cell assay.

IT 261786-27-0P 261786-28-1P 261786-29-2P

261786-30-5P 261786-31-6P 261919-06-6P

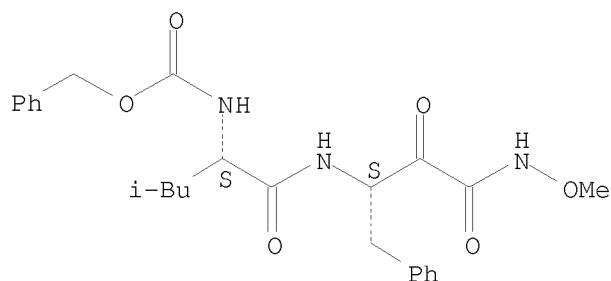
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of potent peptide  $\alpha$ -ketohydroxamate inhibitors of recombinant human calpain I)

RN 261786-27-0 CAPLUS

CN 10-Oxa-2,5,9-triazaundecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, phenylmethyl ester,  
(3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.

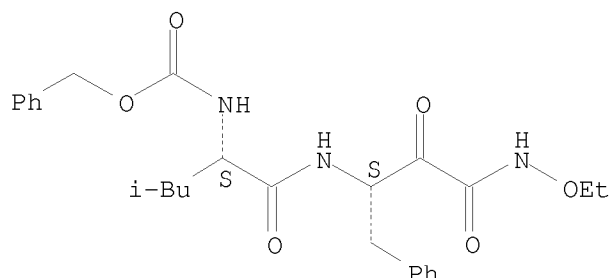


RN 261786-28-1 CAPLUS

CN 10-Oxa-2,5,9-triazadodecanoic acid,

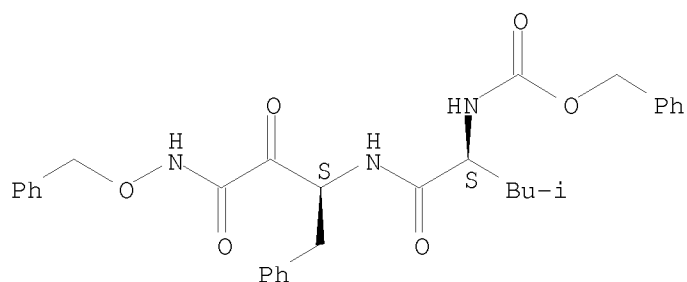
3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, phenylmethyl ester,  
(3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



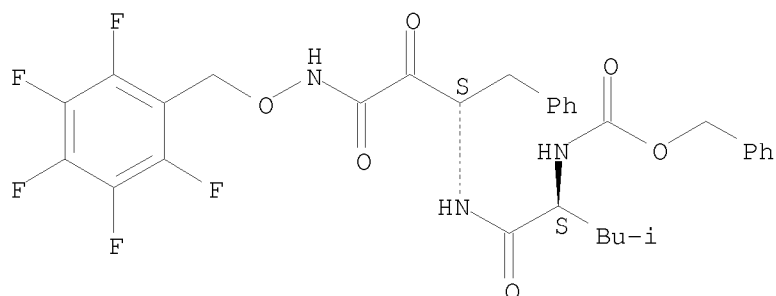
RN 261786-29-2 CAPLUS  
CN 10-Oxa-2,5,9-triazaundecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-11-phenyl-6-(phenylmethyl)-, phenylmethyl  
ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



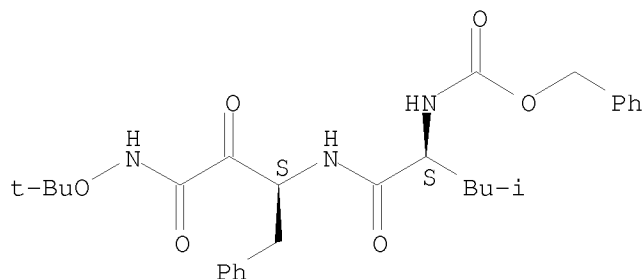
RN 261786-30-5 CAPLUS  
CN 10-Oxa-2,5,9-triazaundecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-11-(2,3,4,5,6-pentafluorophenyl)-6-  
(phenylmethyl)-, phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 261786-31-6 CAPLUS  
CN 10-Oxa-2,5,9-triazadodecanoic acid,  
11,11-dimethyl-3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-,  
phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

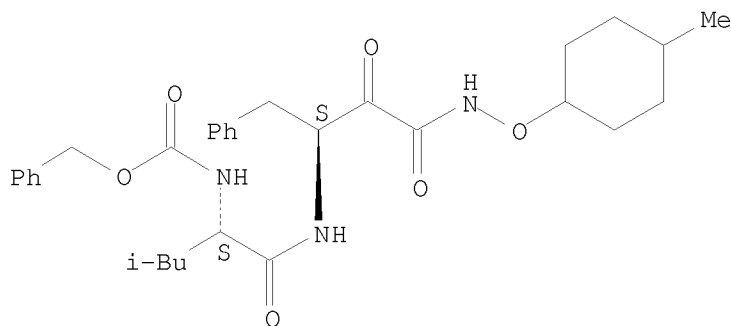
Absolute stereochemistry.



RN 261919-06-6 CAPLUS

CN Carbamic acid, [3-methyl-1-[[[(1S)-3-[[[4-methylcyclohexyl]oxy]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:478119 CAPLUS

DOCUMENT NUMBER: 135:298155

TITLE: Significance of Hydrogen Bonding at the S1' Subsite of Calpain I

AUTHOR(S): Donkor, I. O.; Zheng, X.; Han, J.; Lacy, C.; Miller, D.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, The University of Tennessee, Memphis, TN, 38163, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(13), 1753-1755

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:298155

AB  $\alpha$ -Ketohydroxamates were synthesized as bioisosteres of  $\alpha$ -ketoamides. The  $\alpha$ -ketohydroxamates were generally more potent than the corresponding  $\alpha$ -ketoamides. The potency of the compds. suggests that hydrogen bonding and steric bulk of substituents on the nitrogen atom of the ketoamide moiety influence calpain inhibition.

IT 144231-75-4P 144248-93-1P 144248-94-2P  
261786-28-1P 261786-29-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU

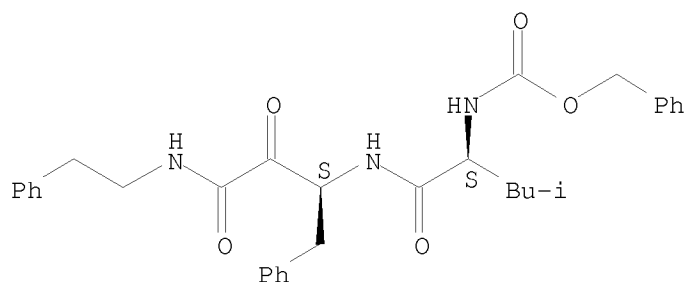
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of  $\alpha$ -ketohydroxamates as calpain inhibitors and significance of hydrogen bonding at S1' subsite of calpain I)

RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

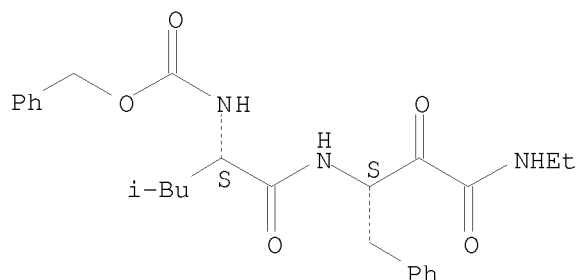
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

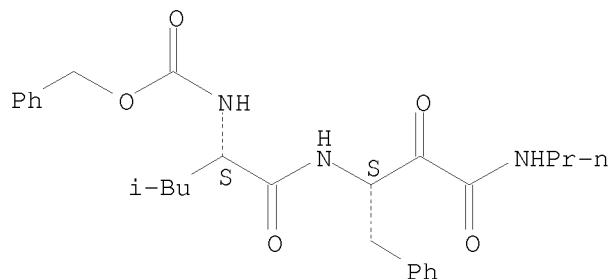
Absolute stereochemistry.



RN 144248-94-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

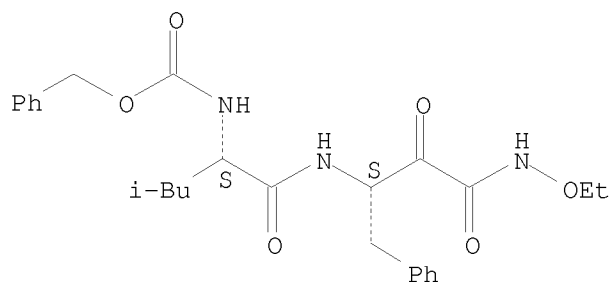
Absolute stereochemistry.



RN 261786-28-1 CAPLUS

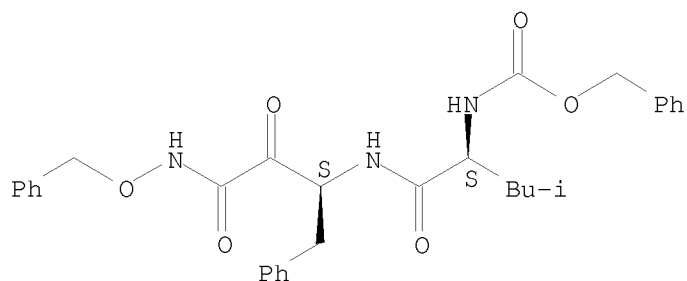
CN 10-Oxa-2,5,9-triazadodecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, phenylmethyl ester,  
(3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 261786-29-2 CAPLUS  
CN 10-Oxa-2,5,9-triazaundecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-11-phenyl-6-(phenylmethyl)-, phenylmethyl  
ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.

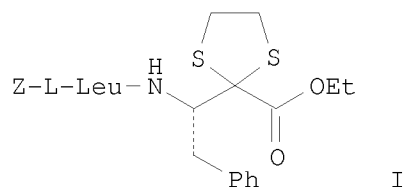


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2001:366736 CAPLUS  
DOCUMENT NUMBER: 134:340711  
TITLE: Preparation of tripeptide  $\alpha$ -ketoamides as serine  
and cysteine protease inhibitors  
INVENTOR(S): Powers, James C.  
PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA  
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. 5,650,508.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6235929	B1	20010522	US 1996-777354	19961227 <--
US 5650508	A	19970722	US 1995-539944	19951006 <--
PRIORITY APPLN. INFO.:			US 1991-815073	B1 19911227 <--
			US 1993-118997	B1 19930909 <--
			US 1994-246511	B1 19940520 <--
			US 1995-539944	A2 19951006 <--

OTHER SOURCE(S): MARPAT 134:340711  
GI



AB Tripeptide  $\alpha$ -ketoamides M1-AA1-AA2-AA3-CONR3R4 [M1 = H, NH<sub>2</sub>CO, NH<sub>2</sub>CS, NH<sub>2</sub>SO<sub>2</sub>, XNHCO, X<sub>2</sub>NCO, XNHCS, X<sub>2</sub>NCS, XNHSO<sub>2</sub>, X<sub>2</sub>NSO<sub>2</sub>, XCO, XCS, XSO<sub>2</sub>, XO<sub>2</sub>C, XOCS; X = (un)substituted C1-10 alkyl or fluoroalkyl, 1-adamantyl, 9-fluorenyl, (un)substituted Ph or naphthyl; AA1 and AA2 = independently side-chain (un)blocked amino acid selected from alanine, valine, leucine, isoleucine, glycine, serine, aspartic acid, and glutamic acid; AA3 = aspartic or glutamic acid; R3 = alkyl or cycloalkyl substituted by Ph and optionally other substituents; R4 = H, alkyl or cycloalkyl which may have a Ph group and other substituents] were prepared as serine and cysteine protease inhibitors. Thus, condensation of protected peptidyl ketoester I (Z = PhCH<sub>2</sub>O<sub>2</sub>C) (prepared in 3 steps from Z-Leu-Phe-OH, Et oxalyl chloride, and 1,2-ethanedithiol) with alkylamines RNH<sub>2</sub> (R = Et, Pr, Bu, Bu-i, CH<sub>2</sub>Ph, CH<sub>2</sub>CH<sub>2</sub>Ph) gave peptidyl ketoamides Z-Leu-Phe-CONHR (II). Peptidyl ketoamides II inhibited chymotrypsin with K<sub>i</sub> = 8-73  $\mu$ M and had half-lives in liver and plasma of >60.

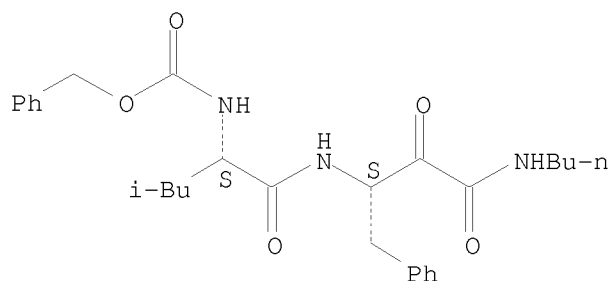
IT 144231-72-1P 144231-73-2P 144231-74-3P  
144231-75-4P 144231-76-5P 144231-77-6P  
144231-78-7P 144231-79-8P 144231-80-1P  
144231-81-2P 144231-82-3P 144231-83-4P  
144231-84-5P 144231-85-6P 144248-93-1P  
144248-94-2P 144248-95-3P 144248-96-4P  
144863-87-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of peptide ketoamides as serine and cysteine protease inhibitors)

RN 144231-72-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

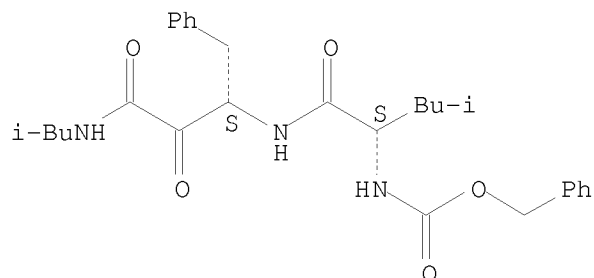


RN 144231-73-2 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-[(2-methylpropyl)amino]-2,3-

dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

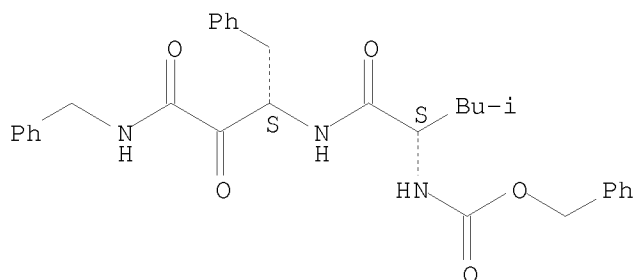
Absolute stereochemistry.



RN 144231-74-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

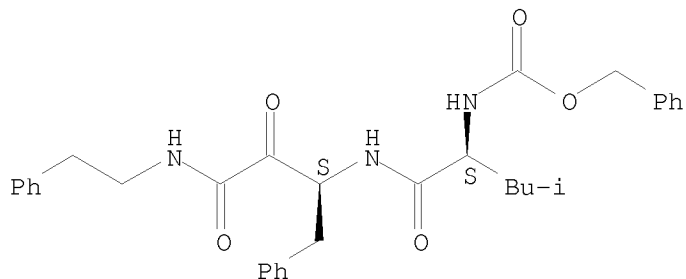
Absolute stereochemistry.



RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

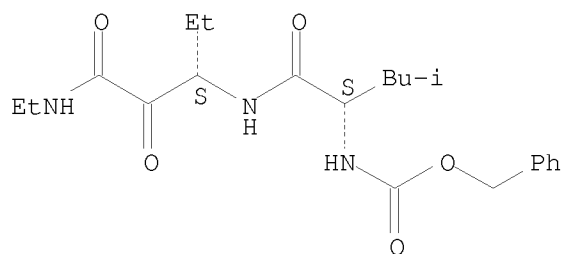


RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

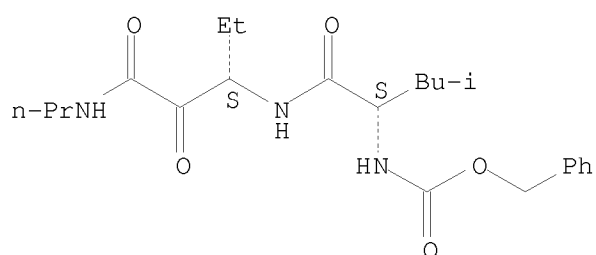
Absolute stereochemistry.





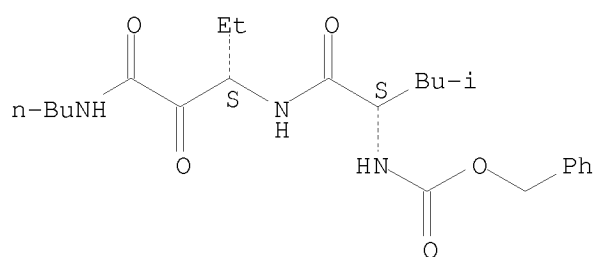
RN 144231-77-6 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



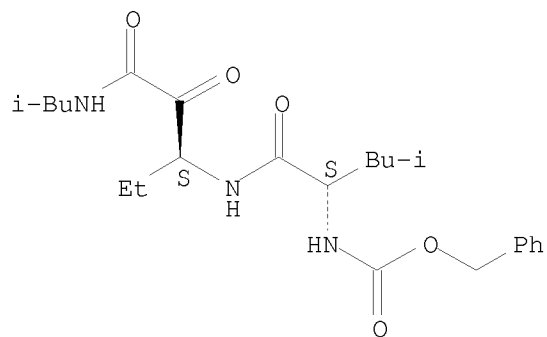
RN 144231-78-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



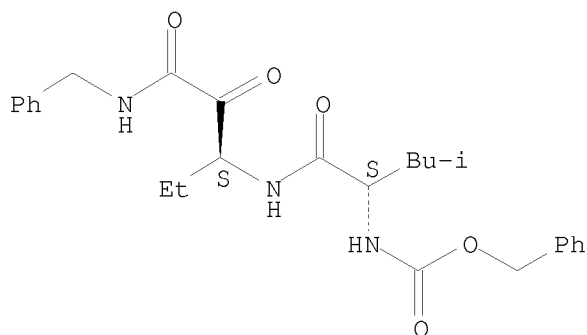
RN 144231-79-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



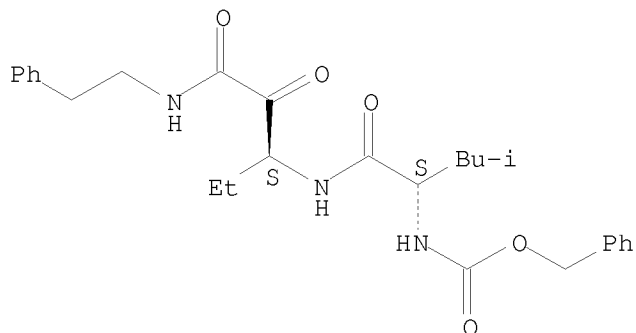
RN 144231-80-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



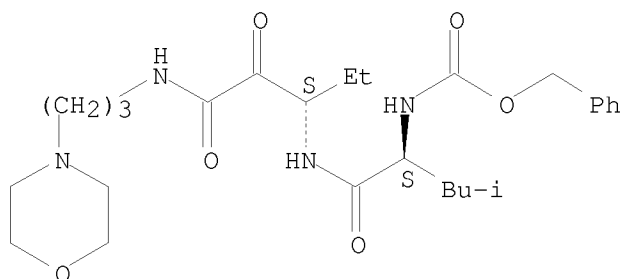
RN 144231-81-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144231-82-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

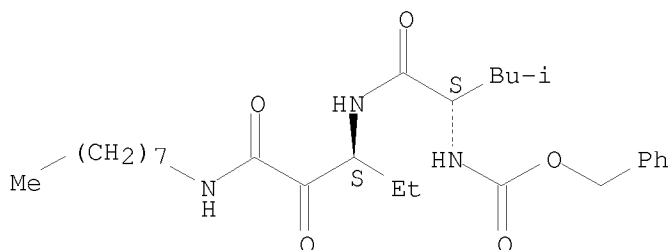
Absolute stereochemistry.



RN 144231-83-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

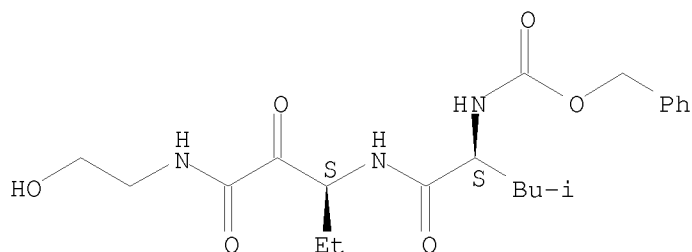
Absolute stereochemistry.



RN 144231-84-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

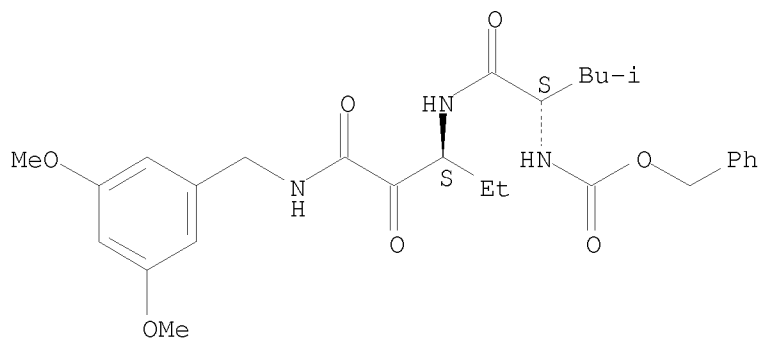
Absolute stereochemistry.



RN 144231-85-6 CAPLUS

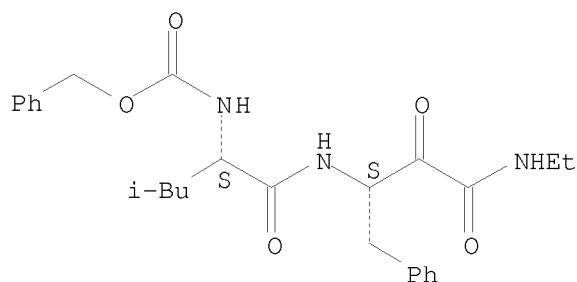
CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



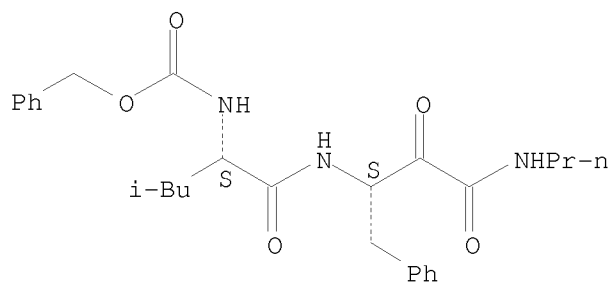
RN 144248-93-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



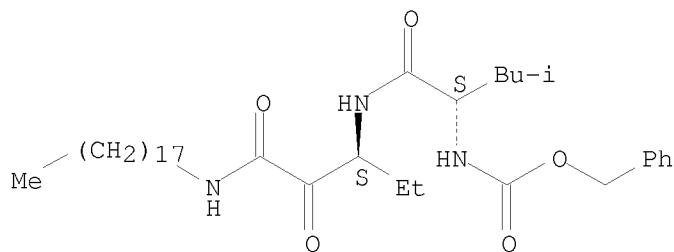
RN 144248-94-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



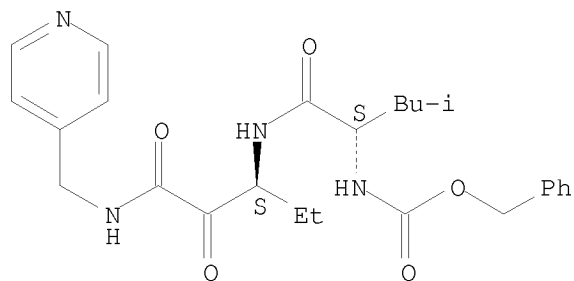
RN 144248-95-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octadecylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



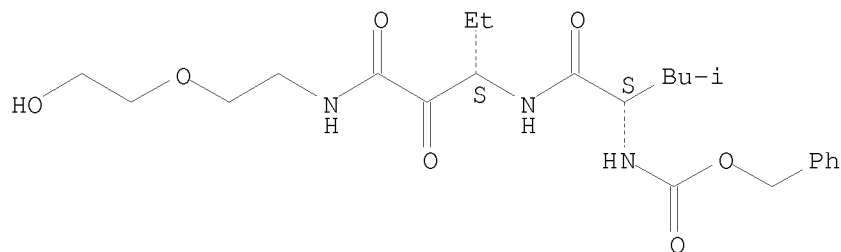
RN 144248-96-4 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144863-87-6 CAPLUS  
 CN 12-Oxa-2,5,9-triazatetradecanoic acid, 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2000:889075 CAPLUS  
 DOCUMENT NUMBER: 134:216845  
 TITLE: Calpain inhibition protects against virus-induced apoptotic myocardial injury  
 AUTHOR(S): DeBiasi, Roberta L.; Edelstein, Charles L.; Sherry, Barbara; Tyler, Kenneth L.  
 CORPORATE SOURCE: Departments of Pediatric Infectious Diseases, Neurology, Denver Veterans Affairs Medical Center, University of Colorado Health Sciences Center, Denver,

CO, 80262, USA  
SOURCE: Journal of Virology (2001), 75(1), 351-361  
CODEN: JOVIAM; ISSN: 0022-538X  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Viral myocarditis is an important cause of human morbidity and mortality for which reliable and effective therapy is lacking. Using reovirus strain 8B infection of neonatal mice, a well-characterized exptl. model of direct virus-induced myocarditis, we now demonstrate that myocardial injury results from apoptosis. Proteases play a critical role as effectors of apoptosis. The activity of the cysteine protease calpain increases in reovirus-infected myocardiocytes and can be inhibited by the dipeptide alpha-ketoamide calpain inhibitor Z-Leu-aminobutyric acid-CONH(CH<sub>2</sub>)<sub>3</sub>-morpholine (CX295). Treatment of reovirus-infected neonatal mice with CX295 protects them against reovirus myocarditis as documented by (i) a dramatic reduction in histopathol. evidence of myocardial injury, (ii) complete inhibition of apoptotic myocardial cell death as identified by terminal deoxynucleotidyltransferase-mediated dUTP-biotin nick end labeling, (iii) a reduction in serum creatine phosphokinase, and (iv) improved weight gain. These findings are the first evidence for the importance of a calpain-associated pathway of apoptotic cell death in viral disease. Inhibition of apoptotic signaling pathways may be an effective strategy for the treatment of viral disease in general and viral myocarditis in particular.

IT 160399-35-9, CX 295

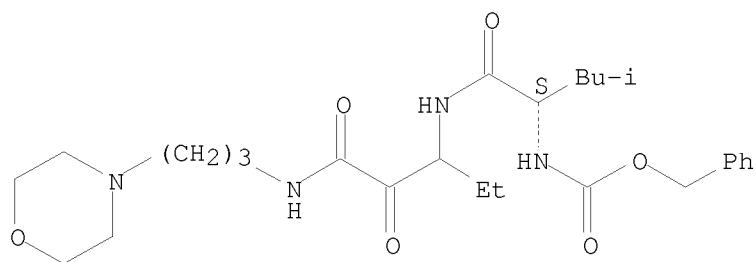
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(calpain inhibition protects against virus-induced apoptotic myocardial injury)

RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Currently available stereo shown.



REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

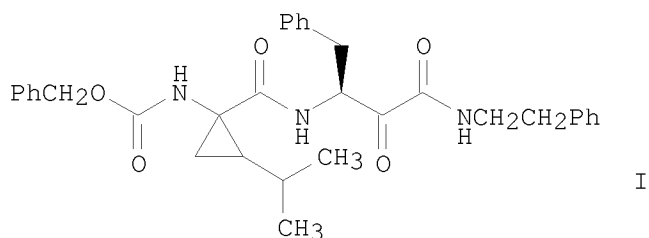
ACCESSION NUMBER: 2000:844921 CAPLUS

DOCUMENT NUMBER: 134:86534

TITLE: Synthesis and calpain inhibitory activity of  $\alpha$ -ketoamides with 2,3-methanoleucine stereoisomers at the P2 position

AUTHOR(S): Donkor, Isaac O.; Zheng, Xiaozhang; Miller, Duane D.  
CORPORATE SOURCE: Department of Pharmaceutical Sciences, The University of Tennessee Health Science Center, Memphis, TN,

SOURCE: 38163, USA  
 Bioorganic & Medicinal Chemistry Letters (2000  
 ), 10(22), 2497-2500  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 134:86534  
 GI



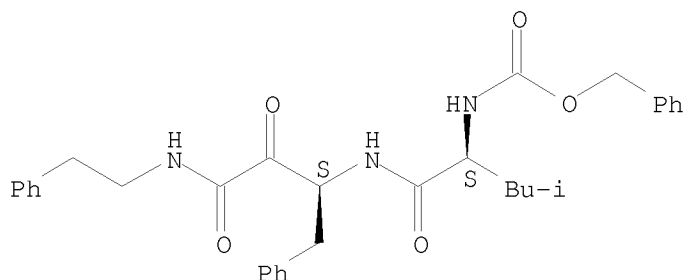
AB A series of novel ketoamides I, (Ph = phenyl) incorporating all four 2,3-methanoleucine stereoisomers at the P2 position, was synthesized. The compds. displayed a wide variation in  $K_i$  values for inhibition of calpain I depending on the configuration of the P2 methanoleucine residue. However, similar variation in cathepsin B inhibition was not observed suggesting that the S2 pocket of calpain I is more stereosensitive than that of cathepsin B.

IT 144231-75-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (synthesis and calpain inhibitory activity of  $\alpha$ -ketoamides with 2,3-methanoleucine stereoisomers at the P2 position)

RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:614463 CAPLUS

DOCUMENT NUMBER: 133:290913

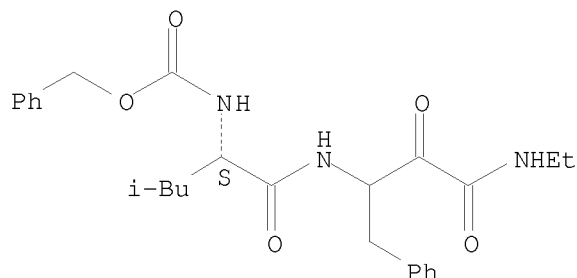
TITLE: Efficacy of novel calpain inhibitors in preventing renal cell death

AUTHOR(S): Harriman, Jay F.; Waters-Williams, Shayla; Chu, Der-Lun; Powers, James C.; Schnellmann, Rick G.  
 CORPORATE SOURCE: Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences, Little Rock, AR, USA  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 294(3), 1083-1087  
 CODEN: JPETAB; ISSN: 0022-3565  
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Inhibitors of calpains, calcium-activated neutral proteases, protect against cell death produced by anoxia and a variety of toxicants both in vitro and in vivo. The problems with known calpain inhibitors are a lack of specificity, low membrane permeability, and/or low potency. The goal of this study was to determine the effects of seven novel dipeptide and tripeptide calpain inhibitors on calpain activity and antimycin A-induced cell death in rabbit renal proximal tubule (RPT) suspensions. We chose the compds. based on their inhibitory consts. for  $\mu$ -vs. m-calpain, specificity of the inhibitors for calpain, and membrane permeability. Only three of the compds. inhibited calpain in RPT and were cytoprotective (Z-Leu-Phe-COOH, Z-Leu-Abu-CONH-CH<sub>2</sub>-CH(OH)-Ph, and Z-Leu-Phe-CONH-Et). Interestingly, Z-Leu-Phe-COOEt, Z-Leu-Abu-CONH-CH<sub>2</sub>-CH(OH)-C<sub>6</sub>F<sub>5</sub>, and Z-Leu-Abu-CONH-CH<sub>2</sub>-2-quinolinyl were greater than 60% cytoprotective but did not inhibit calpain in RPT. Z-Leu-Abu-CONH(CH<sub>2</sub>)<sub>3</sub>-morpholine was neither cytoprotective nor inhibited calpain. Although these results suggest that six of the seven peptide calpain inhibitors are cell permeable, only three of them inhibited calpain activity in RPT and were cytoprotective. Their ability to inhibit calpain or produce cytoprotection did not correlate with their ability to selectively inhibit purified  $\mu$ - or m-calpain. Thus it remains to be determined whether they inhibit  $\mu$ -calpain, m-calpain, or both in RPT. These results also suggest that inhibition of other protease(s) in addition to calpains may be responsible for the cytoprotective actions of some compds.

IT 150957-45-2 160399-35-9 207456-33-5  
 301295-26-1 301295-27-2  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (efficacy of novel calpain inhibitors in inhibiting renal proximal tubule  $\mu$ - and m- calpain activity and cell death)  
 RN 150957-45-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

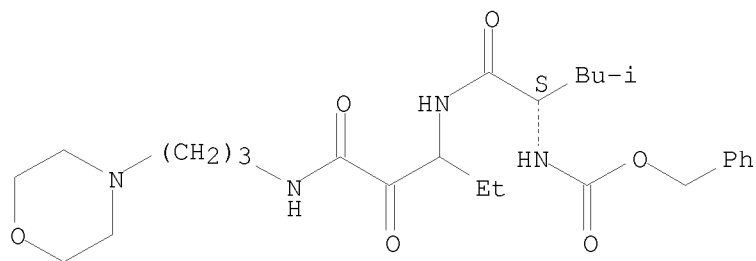


RN 160399-35-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA



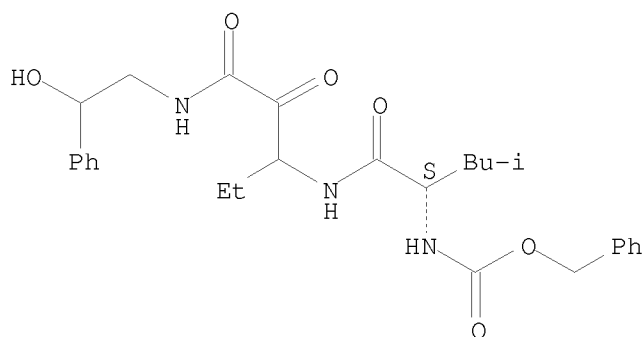
INDEX NAME)

Absolute stereochemistry.  
Currently available stereo shown.



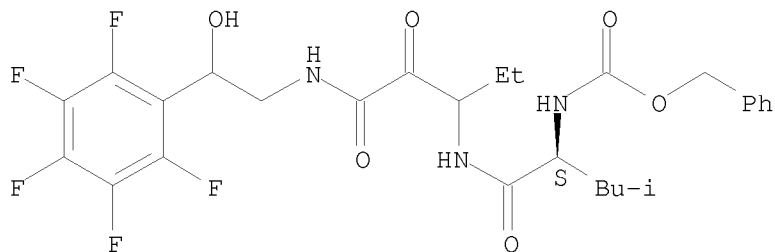
RN 207456-33-5 CAPLUS  
CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



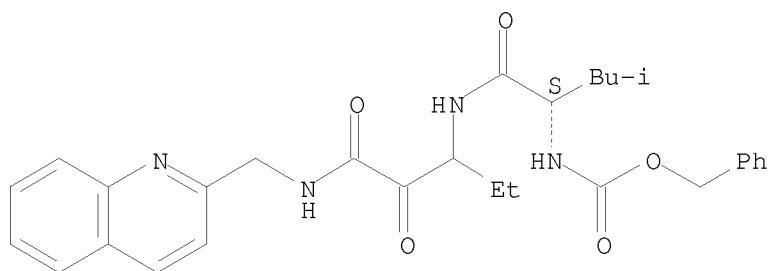
RN 301295-26-1 CAPLUS  
CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[2-hydroxy-2-(2,3,4,5,6-pentafluorophenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 301295-27-2 CAPLUS  
CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:350709 CAPLUS

DOCUMENT NUMBER: 133:208170

TITLE: Passerini multicomponent reaction of protected  $\alpha$ -amino aldehydes as a tool for combinatorial synthesis of enzyme inhibitors

AUTHOR(S): Banfi, Luca; Guanti, Giuseppe; Riva, Renata  
CORPORATE SOURCE: Dip. Chim. Chim. Ind., Univ. Genoa, C.N.R., CSCCCA, Genoa, Italy

SOURCE: Chemical Communications (Cambridge) (2000), (11), 985-986

CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:208170

AB Three-component Passerini condensation of N-Boc- $\alpha$ -amino aldehydes with various isocyanides and carboxylic acids leads, after Boc-deprotection/transacylation, to complex peptide-like structures containing an  $\alpha$ -hydroxy  $\beta$ -amino acid unit or, after oxidation, an  $\alpha$ -oxo  $\beta$ -amino acid unit.

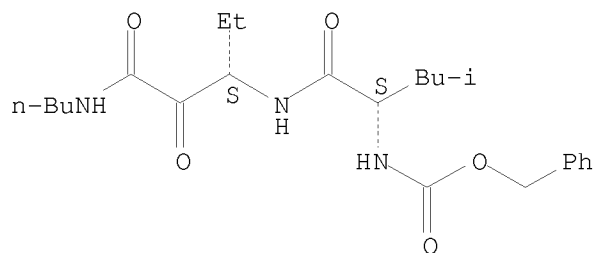
IT 144231-78-7P 289708-28-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of peptidomimetics by Passerini multicomponent reaction of protected  $\alpha$ -amino aldehydes)

RN 144231-78-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

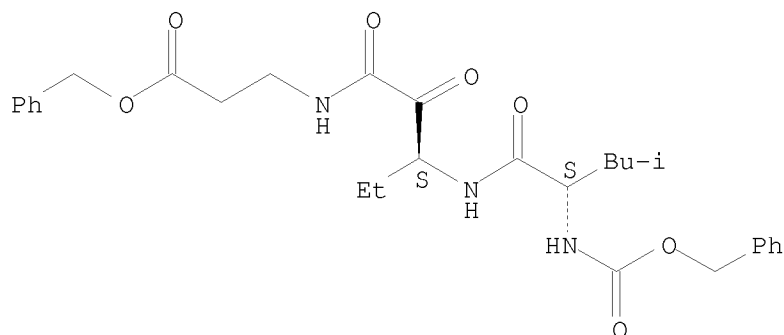
Absolute stereochemistry.



RN 289708-28-7 CAPLUS

CN 13-Oxa-4,8,11-triazatetradecanoic acid, 7-ethyl-10-(2-methylpropyl)-5,6,9,12-tetraoxo-14-phenyl-, phenylmethyl ester, (7S,10S)- (CA INDEX NAME)

Absolute stereochemistry.

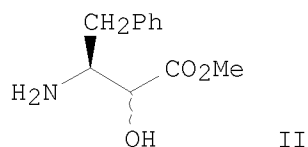
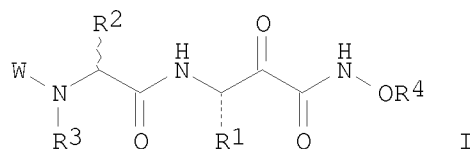


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2000:209900 CAPLUS  
DOCUMENT NUMBER: 132:237376  
TITLE: Preparation of hydroxamate-containing peptides as cysteine and serine protease inhibitors  
INVENTOR(S): Mallamo, John P.; Bihovsky, Ron; Josef, Kurt Allen  
PATENT ASSIGNEE(S): Cephalon, Inc., USA  
SOURCE: PCT Int. Appl., 35 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000016767	A1	20000330	WO 1999-US21664	19990920 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6686335	B1	20040203	US 1999-398562	19990917 <--
CA 2342985	A1	20000330	CA 1999-2342985	19990920 <--
AU 9960502	A	20000410	AU 1999-60502	19990920 <--
AU 771518	B2	20040325		
EP 1115390	A1	20010718	EP 1999-969333	19990920 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 510303	A	20021220	NZ 1999-510303	19990920 <--
JP 2003534233	T	20031118	JP 2000-573728	19990920 <--
CN 1212835	C	20050803	CN 1999-811251	19990920 <--
NO 2001001388	A	20010516	NO 2001-1388	20010319 <--
US 20040106558	A1	20040603	US 2003-717773	20031120 <--
US 7060683	B2	20060613		
PRIORITY APPLN. INFO.:			US 1998-101414P	P 19980922 <--
			US 1999-398562	A 19990917 <--
			WO 1999-US21664	W 19990920 <--
OTHER SOURCE(S):		MARPAT 132:237376		

GI



AB Hydroxamate-containing peptides I [W is A-B-D; A is (un)substituted aryl(CH<sub>2</sub>)<sub>n</sub>, heteroaryl(CH<sub>2</sub>)<sub>n</sub> (n = 0-6), alkyl, alkenyl or cycloalkyl; B is a bond, CO, SO, SO<sub>2</sub>, OCO, NR<sub>5</sub>CO, NR<sub>5</sub>SO<sub>2</sub>, or NR<sub>5</sub>SO; D is a bond, an amino acid residue or a peptide; R<sub>1</sub>-R<sub>5</sub> are H or (un)substituted alkyl or cycloalkyl] have been prepared as inhibitors of cysteine and serine proteases. Thus, Cbz-Leu-Phe-CONHOMe (Cbz = benzyloxycarbonyl), prepared by coupling of Cbz-Leu-OH with II.HCl, followed by amidation with H<sub>2</sub>NOMe.HCl and Dess-Martin oxidation, showed IC<sub>50</sub> = 10 nM for inhibition of caplain activity.

IT 261786-27-0P 261786-28-1P 261786-29-2P  
261786-30-5P 261786-31-6P 261786-43-0P  
261919-06-6P

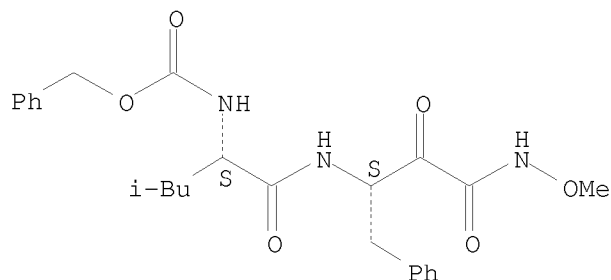
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamate containing cysteine and serine protease inhibitors)

RN 261786-27-0 CAPLUS

CN 10-Oxa-2,5,9-triazaundecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, phenylmethyl ester,  
(3S,6S)- (CA INDEX NAME)

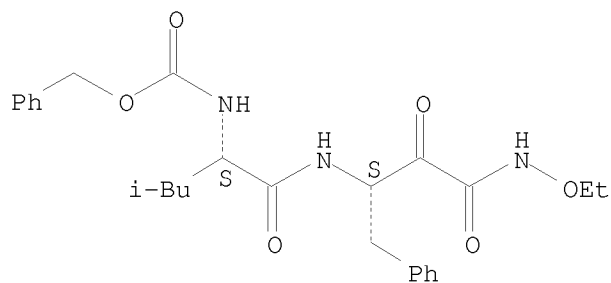
Absolute stereochemistry.



RN 261786-28-1 CAPLUS

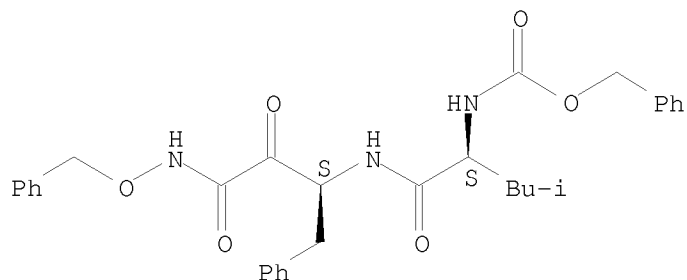
CN 10-Oxa-2,5,9-triazadodecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, phenylmethyl ester,  
(3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



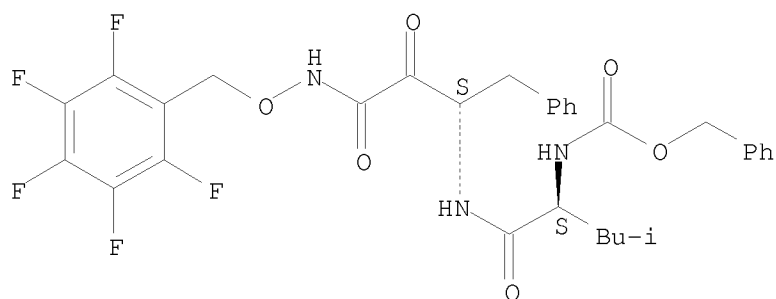
RN 261786-29-2 CAPLUS  
CN 10-Oxa-2,5,9-triazaundecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-11-phenyl-6-(phenylmethyl)-, phenylmethyl  
ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



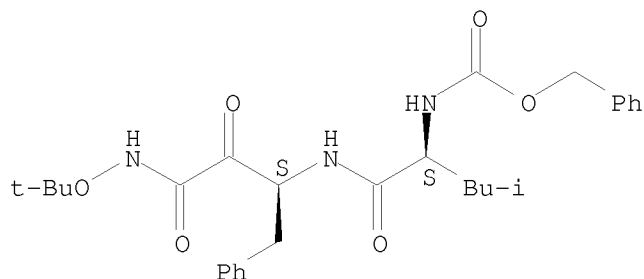
RN 261786-30-5 CAPLUS  
CN 10-Oxa-2,5,9-triazaundecanoic acid,  
3-(2-methylpropyl)-4,7,8-trioxo-11-(2,3,4,5,6-pentafluorophenyl)-6-(  
phenylmethyl)-, phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



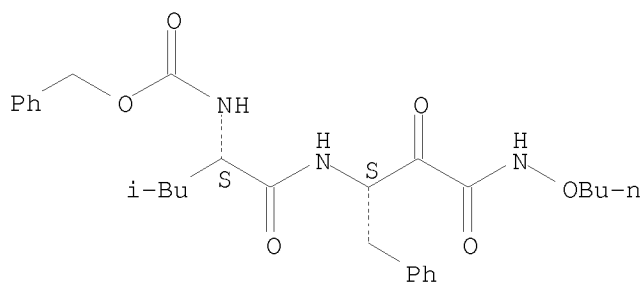
RN 261786-31-6 CAPLUS  
CN 10-Oxa-2,5,9-triazadodecanoic acid,  
11,11-dimethyl-3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-,  
phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



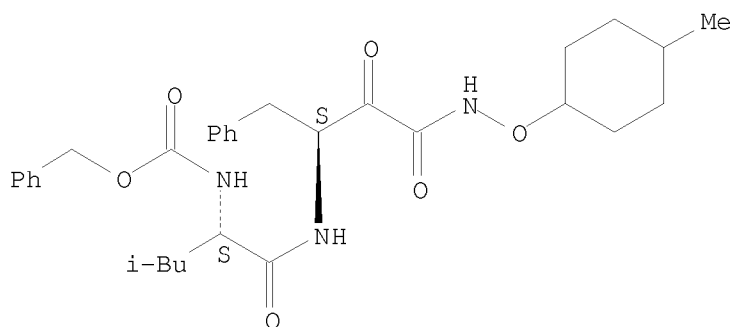
RN 261786-43-0 CAPLUS  
 CN 10-Oxa-2,5,9-triazatetradecanoic acid,  
 3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, phenylmethyl ester,  
 (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 261919-06-6 CAPLUS  
 CN Carbamic acid, [3-methyl-1-[[[(1S)-3-[[[4-methylcyclohexyl]oxy]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:109998 CAPLUS

DOCUMENT NUMBER: 133:38070

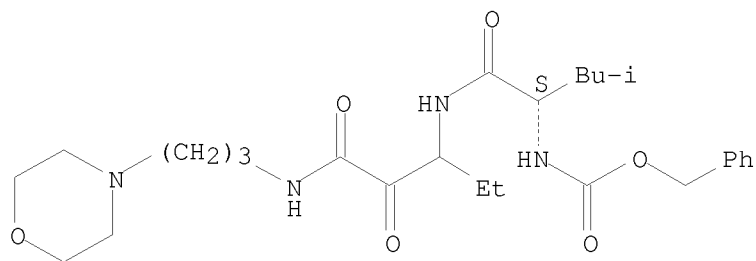
TITLE: Behavioral efficacy of posttraumatic calpain inhibition is not accompanied by reduced spectrin proteolysis, cortical lesion, or apoptosis

AUTHOR(S): Saatman, Kathryn E.; Zhang, Chen; Bartus, Raymond T.; McIntosh, Tracy K.  
 CORPORATE SOURCE: Department of Neurosurgery, University of Pennsylvania, Philadelphia, PA, 19104, USA  
 SOURCE: Journal of Cerebral Blood Flow and Metabolism (2000), 20(1), 66-73  
 CODEN: JCBMDN; ISSN: 0271-678X  
 PUBLISHER: Lippincott Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Administration of the selective calpain inhibitor AK295 has been shown to attenuate motor and cognitive dysfunction after brain trauma in rats. To explore mechanisms underlying the behavioral efficacy of posttraumatic calpain inhibition, the histol. consequences of AK295 administration were investigated. Rats received lateral fluid percussion brain injury of moderate severity (2.2-2.4 atm) or served as uninjured controls. Fifteen min after injury, the animals received a 48-h infusion of either 2 mM AK295 (120-140 mg/kg) or saline via the carotid artery. Forty-eight h and 1 wk after injury, spectrin fragments generated specifically by calpain were detected in saline-treated, brain-injured animals. Equivalent spectrin breakdown was observed in the cortex and hippocampus of AK295-treated animals. Similarly, administration of the calpain inhibitor did not attenuate cortical lesion size or the nos. of apoptotic cells in the cortex, subcortical white matter, or hippocampus, 48 h after injury. These data suggest that an overt reduction in spectrin proteolysis, cortical lesion, or apoptotic cell death after 48 h or 1 wk is not required for the behavioral improvements associated with calpain inhibition by AK295 after exptl. brain injury in rats.

IT 160399-35-9, AK 295  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (calpain inhibitor AK 295 effect on spectrin proteolysis, cortical lesions, and apoptosis after brain injury)  
 RN 160399-35-9 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Currently available stereo shown.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:249093 CAPLUS

DOCUMENT NUMBER: 130:312099

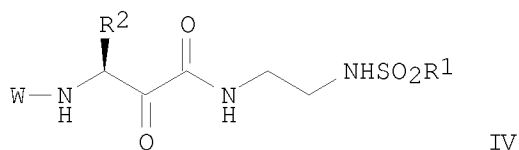
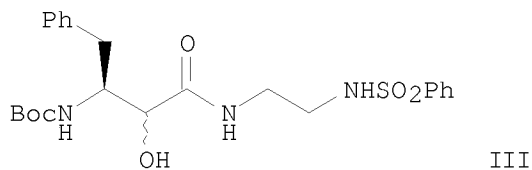
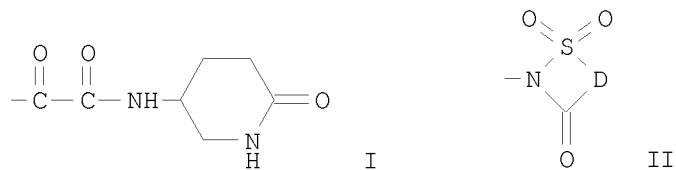
TITLE: Preparation of peptide-containing  $\alpha$ -ketoamide cysteine and serine protease inhibitors

INVENTOR(S): Chatterjee, Sankar; Mallamo, John P.; Bihovsky, Ron; Wells, Gregory J.

PATENT ASSIGNEE(S): Cephalon Inc., USA  
 SOURCE: PCT Int. Appl., 56 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917790	A1	19990415	WO 1998-US21055	19981007 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6150378	A	20001121	US 1998-166808	19981006 <--
CA 2304116	A1	19990415	CA 1998-2304116	19981007 <--
AU 9910686	A	19990427	AU 1999-10686	19981007 <--
AU 749555	B2	20020627		
EP 1021199	A1	20000726	EP 1998-953275	19981007 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001518513	T	20011016	JP 2000-514661	19981007 <--
NZ 503550	A	20020201	NZ 1998-503550	19981007 <--
CN 1207056	C	20050622	CN 1998-809921	19981007 <--
US 6288231	B1	20010911	US 2000-527540	20000316 <--
MX 200003419	A	20001113	MX 2000-3419	20000407 <--
US 20020055616	A1	20020509	US 2001-879336	20010612 <--
US 6703368	B2	20040309		
US 20040102609	A1	20040527	US 2003-685923	20031014 <--
US 7001907	B2	20060221		
US 20060069037	A1	20060330	US 2005-273850	20051115 <--
PRIORITY APPLN. INFO.:				
			US 1997-61309P	P 19971007 <--
			US 1998-166808	A 19981006 <--
			WO 1998-US21055	W 19981007 <--
			US 2000-527540	A3 20000316 <--
			US 2001-879336	A3 20010612 <--
			US 2003-685923	A3 20031014 <--
OTHER SOURCE(S):				
GI				
MARPAT 130:312099				





AB Title compds. of formula Q-(Aaa)n-(NR3-CH(R1)-CO)q-NH-CH(R2)-Z [Q = G-B-(CHR4)v; R4 = H, C1-4 alkyl; v = 0-2; B = CO, OC(O), S(O)m, CH2, bond, NR5CO, S(O)m-A-CO, CO-A-CO; R5 = H, alkyl; m = 0-2; A = (un)substituted alkylene or cycloalkylene; G = H, a blocking group, alkenyl, (un)substituted alkyl, aryl, heterocyclyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, or arylheteroalkyl; Aaa = an amino acid optionally containing blocking groups; n = 0-3; R1 and R2 = independently H, heteroaryl, (un)substituted alkyl, arylalkyl, heteroalkyl, heteroarylalkyl, or alkoxyalkyl, (un)substituted naturally occurring amino acid side chain; R3 = H, alkyl, arylalkyl, heteroalkyl, heteroarylalkyl, alkoxyalkyl, (un)substituted naturally occurring amino acid side chain, blocking group, etc.; q = 0-1; Z = CO-CO-NH-X-A1-K or I; X = bond, O; A1 = A; K = N(R10)Y, II, SO2N(R8)(R10); D = fused aryl, or heteroaryl group; R11 = alkoxy, aryloxy, NHR12; R9, R12 = H, (un)substituted alkyl, aryl, or heteroaryl; Y = SO2R8, CONHR9, CSNHR9, C(=NCN)R11, C(=NCONHR10)R11, CO2R8; R8 = (un)substituted alkyl, alkoxy, aryl, or heterocyclyl; R10 = H, alkyl; R8 and R10 may combine with the N atom to which they are attached to form an N-containing heterocyclic ring; R9 may be combined with an A1 alkylene group to form an N-containing heterocyclic ring] or their pharmaceutically acceptable salts, were prepared as cysteine and serine protease inhibitors. Thus, III (preparation given) was oxidized by Dess-Martin periodinane, deprotected, and coupled with PhSO2-L-Pro-OH to yield compound IV (W = PhSO2-L-Pro, R2 = PhCH2, R1 = Ph) which exhibited 78% inhibition of calpain I at 10  $\mu$ M. Compound IV (W = MeSO2-D-Ser(CH2Ph), R2 = CH2OMe, R1 = Ph) exhibited 100% inhibition of calpain I at 10  $\mu$ M. Methods for the use of the protease inhibitors are also described.

IT 223512-80-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

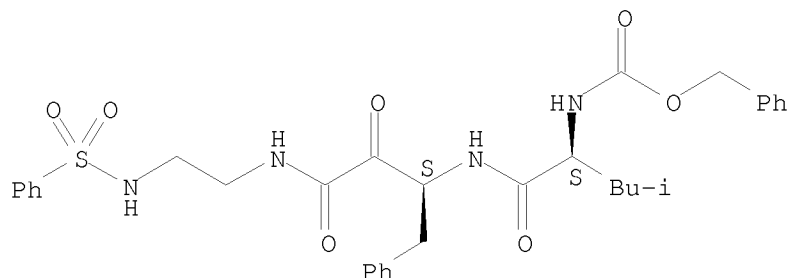
(preparation of peptide-containing  $\alpha$ -ketoamide cysteine and serine protease inhibitors)

RN 223512-80-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[[2-[(phenylsulfonyl)amino]ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-,

phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:744969 CAPLUS

DOCUMENT NUMBER: 130:20593

TITLE: The use of biologically active substances for influencing the extracellular space of sensory cells

INVENTOR(S): Eckmiller, Marion Sangster

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850065	A2	19981112	WO 1998-EP1951	19980402 <--
WO 9850065	A3	19990610		
W:	AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GM, GW, HU, IL, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TT, UA, US, UZ, VN, YU, ZW, AZ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
DE 19718826	A1	19981112	DE 1997-19718826	19970505 <--
CA 2288631	A1	19981112	CA 1998-2288631	19980402 <--
AU 9876417	A	19981127	AU 1998-76417	19980402 <--
EP 980256	A2	20000223	EP 1998-924097	19980402 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRIORITY APPLN. INFO.: DE 1997-19718826 A 19970505 <--  
WO 1998-EP1951 W 19980402 <--

AB The invention relates to the use of an active substance influencing the calcium homeostasis of cells to treat degeneration of sensory cells and adjacent cells. The effect of higher Ca concns. with and without calpain inhibitors on the structure of retinal outer segments was determined

IT 160399-35-9, AK295

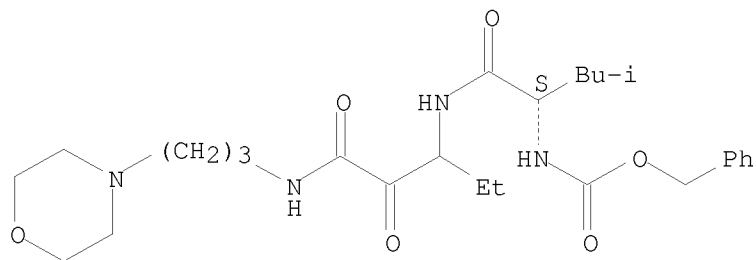
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drugs for influencing extracellular area of sensory cells)

RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Currently available stereo shown.



L10 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:397812 CAPLUS

DOCUMENT NUMBER: 129:54609

ORIGINAL REFERENCE NO.: 129:11385a,11388a

TITLE: Preparation of peptide  $\alpha$ -ketoamides as serine and cysteine protease inhibitors

INVENTOR(S): Powers, James C.

PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA

SOURCE: U.S., 25 pp., Cont.-in-part of U. S. 5,650,508.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

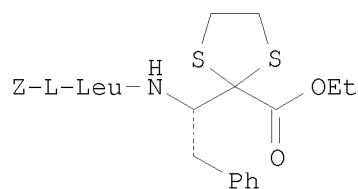
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5763576	A	19980609	US 1996-777208	19961227 <--
US 5650508	A	19970722	US 1995-539944	19951006 <--
PRIORITY APPLN. INFO.:			US 1995-539944	A2 19951006 <--
			US 1991-815073	B1 19911227 <--
			US 1993-118997	B1 19930909 <--
			US 1994-246511	B1 19940520 <--

OTHER SOURCE(S): MARPAT 129:54609  
GI



I

AB Di-, tri-, and tetrapeptide  $\alpha$ -ketoamides M1-AA-NHCHR2COCONR3R4, M1-AA2-AA-CONR3R4, M1-AA1-AA2-AA3-CONR3R4, and M1-AA1-AA2-AA3-AA4-CONR3R4 [M1 = H, NH2CO, NH2CS, NH2SO2, XNHCO, X2NCO, XNHCS, X2NCS, XNHSO2, X2NSO2, XCO, XCS, XSO2, XO2C, XOCS; X = (un)substituted C1-10 alkyl, (un)substituted C1-10 fluoroalkyl, 1-adamantyl, 9-fluorenyl, (un)substituted Ph, (un)substituted naphthyl; AA, AA1, AA2, AA3, AA4 =

independently side-chain (un)blocked amino acid; R2 = C1-8 (un)branched alkyl, C1-8 (un)branched cycloalkyl, C1-8 (un)branched fluoroalkyl; R3, R4 = independently H, C1-20 alkyl, C3-20 cycloalkyl, C1-20 arylalkyl, C1-10 heterocycloalkyl] are useful for selectively inhibiting serine proteases, selectively inhibiting cysteine proteases, generally inhibiting all serine proteases, and generally inhibiting all cysteine proteases. Thus, condensation of protected peptidyl ketoester I (Z = PhCH2O2C) (prepared in 3 steps from Z-Phe-Leu-OH, Et oxalyl chloride, and 1,2-ethanedithiol) with alkylamines RNH2 (R = Et, Pr, Bu, CH2CHMe2, CH2Ph, CH2CH2Ph) gave peptidyl ketoamides Z-Phe-Leu-CONHR (II). Peptidyl ketoamides II inhibited chymotrypsin with Ki = 8-73 mM, and had half-lives in liver and plasma of >60.

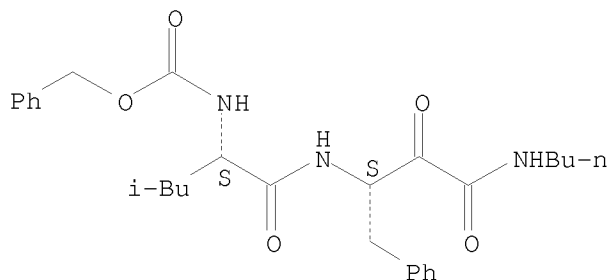
IT 144231-72-1P 144231-73-2P 144231-74-3P  
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 144231-81-2P 144231-82-3P 144231-83-4P  
 144231-84-5P 144231-85-6P 144248-93-1P  
 144248-94-2P 144248-95-3P 144248-96-4P  
 144863-87-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of peptide ketoamides as serine and cysteine protease inhibitors)

RN 144231-72-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

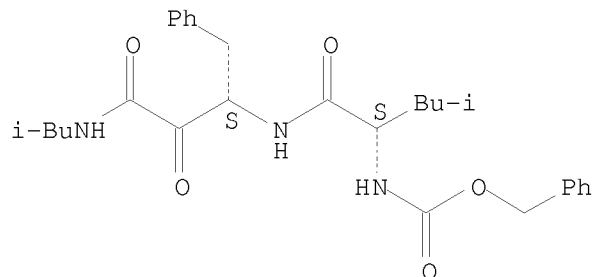
Absolute stereochemistry.



RN 144231-73-2 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-[(2-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

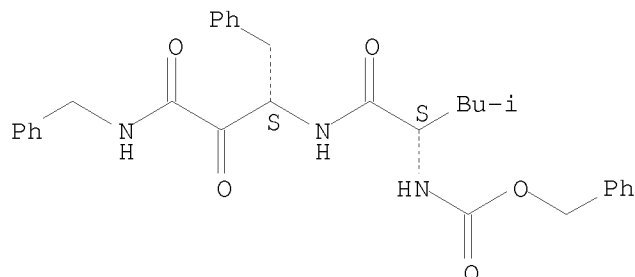
Absolute stereochemistry.



RN 144231-74-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

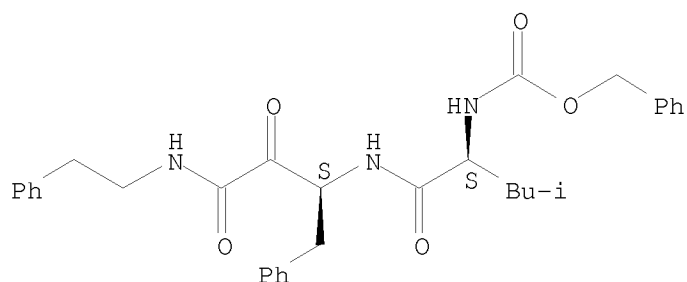
Absolute stereochemistry.



RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

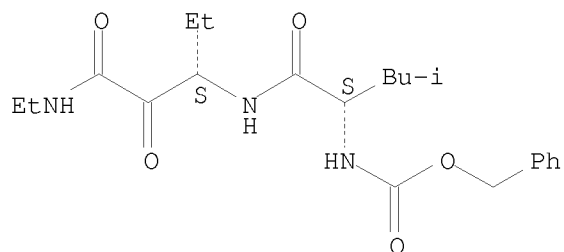
Absolute stereochemistry.



RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

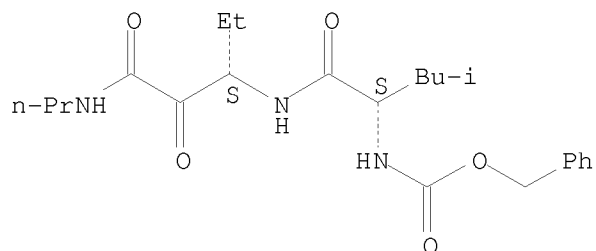
Absolute stereochemistry.



RN 144231-77-6 CAPLUS

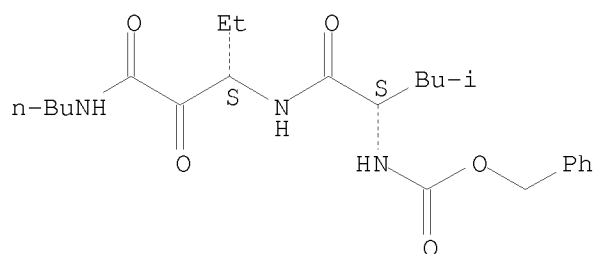
CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



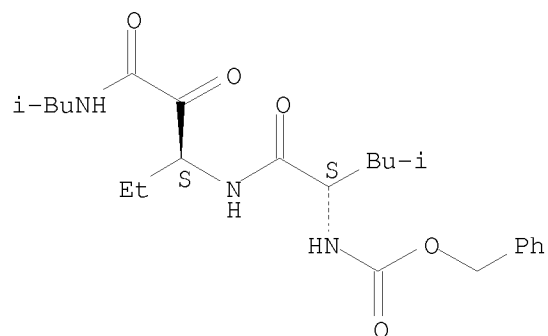
RN 144231-78-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



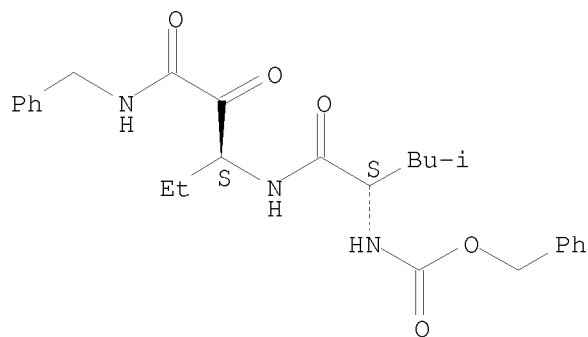
RN 144231-79-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144231-80-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

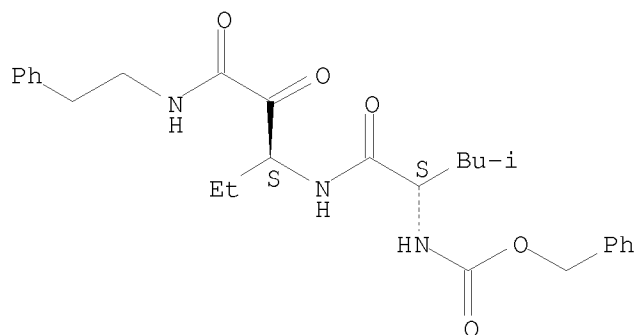
Absolute stereochemistry.



RN 144231-81-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

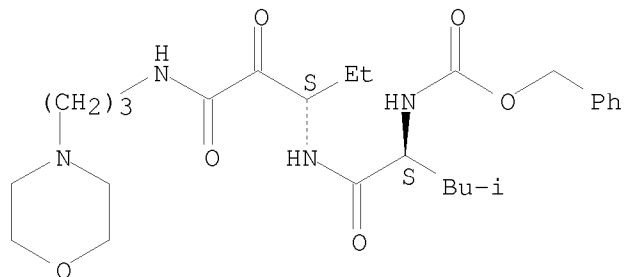
Absolute stereochemistry.



RN 144231-82-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

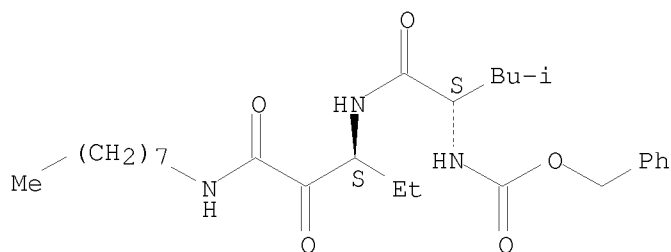
Absolute stereochemistry.



RN 144231-83-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

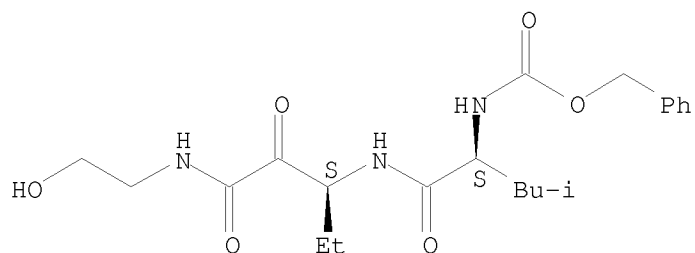
Absolute stereochemistry.



RN 144231-84-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

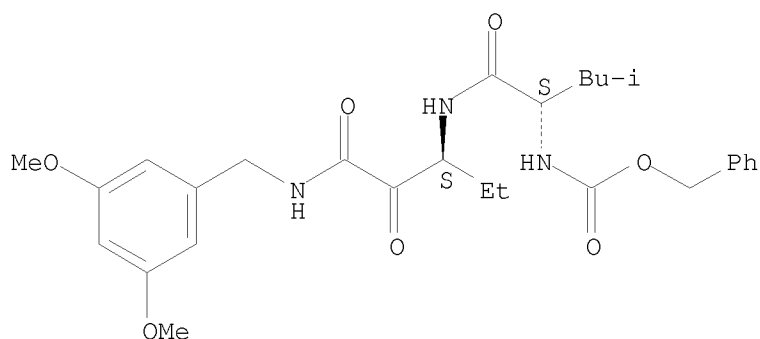
Absolute stereochemistry.



RN 144231-85-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

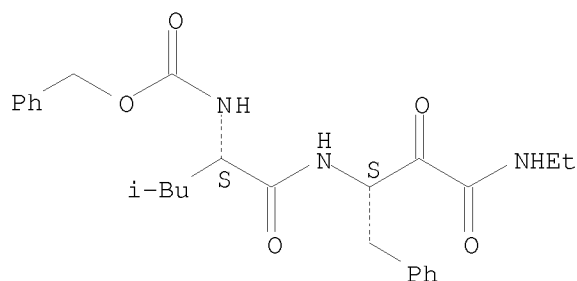


RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

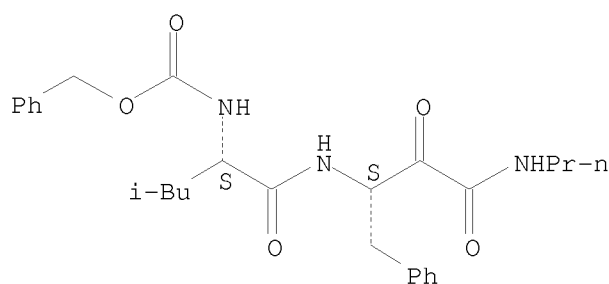




RN 144248-94-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

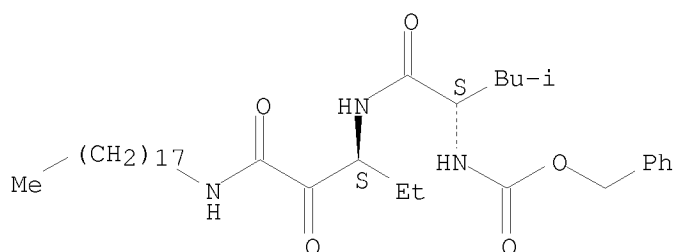
Absolute stereochemistry.



RN 144248-95-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octadecylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

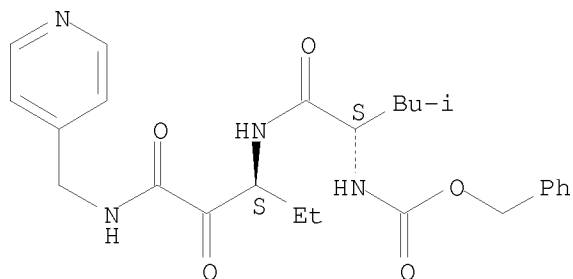
Absolute stereochemistry.



RN 144248-96-4 CAPLUS

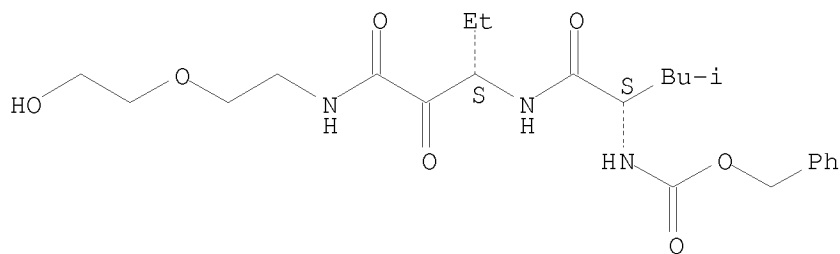
CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144863-87-6 CAPLUS  
 CN 12-Oxa-2,5,9-triazatetradecanoic acid,  
 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester,  
 (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

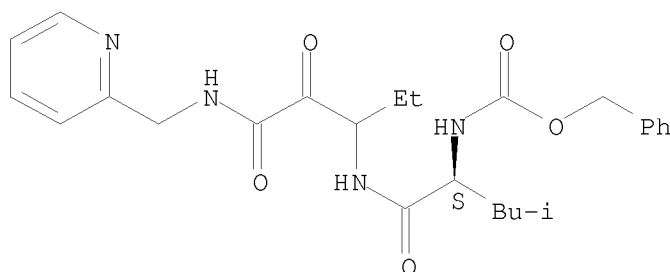
L10 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1998:293392 CAPLUS  
 DOCUMENT NUMBER: 129:8596  
 ORIGINAL REFERENCE NO.: 129:1853a  
 TITLE: The use of calpain inhibitors to treat ocular neural  
 pathology  
 INVENTOR(S): Pang, Iok-Hou; Kapin, Michael A.; Desantis, Louis, Jr.  
 PATENT ASSIGNEE(S): Alcon Laboratories, Inc., USA; Pang, Iok-Hou; Kapin,  
 Michael A.; Desantis, Louis, Jr.  
 SOURCE: PCT Int. Appl., 20 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818485	A1	19980507	WO 1997-US16742	19970919 <--
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9744893	A	19980522	AU 1997-44893	19970919 <--
US 6303579	B1	20011016	US 1999-284074	19990405 <--
PRIORITY APPLN. INFO.:				
			US 1996-29353P	P 19961031 <--
			WO 1997-US16742	W 19970919 <--

AB The invention provides pharmaceutical compns. containing calpain inhibitors  
 and methods of using these calpain inhibitors to prevent or ameliorate  
 ocular neural tissue disease or damage. Example calpain inhibitors are PD

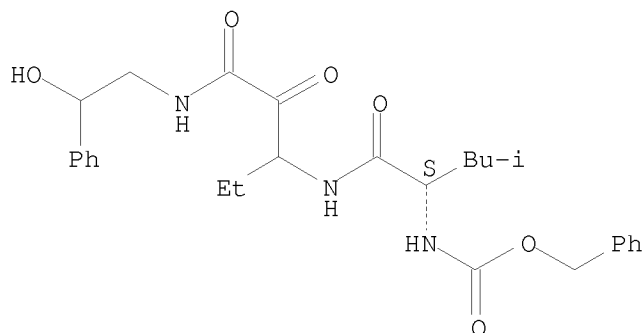
150606 and PhCH2O2C-leucine-norvaline-CONHCH2-2-pyridyl.  
 IT 207456-28-8 207456-33-5 207456-38-0  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (calpain inhibitors to treat ocular neural pathol.)  
 RN 207456-28-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



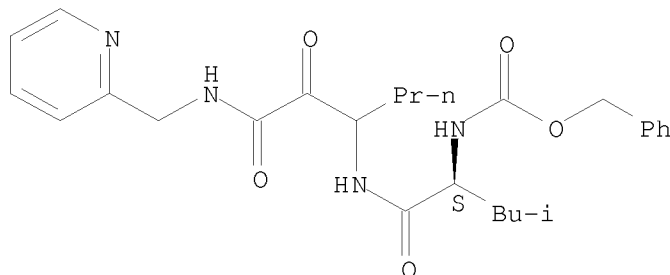
RN 207456-33-5 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 207456-38-0 CAPLUS  
 CN Carbamic acid, [(1S)-3-methyl-1-[[[1-[oxo[(2-pyridinylmethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:72025 CAPLUS

DOCUMENT NUMBER: 128:213211

ORIGINAL REFERENCE NO.: 128:42097a,42100a

TITLE: New inhibitors of calpain prevent degradation of cytoskeletal and myelin proteins in spinal cord in vitro

AUTHOR(S): James, T.; Matzelle, D.; Bartus, R.; Hogan, E. L.; Banikl, N. L.

CORPORATE SOURCE: Department of Neurology, Medical University of South Carolina, Charleston, SC, USA

SOURCE: Journal of Neuroscience Research (1998), 51(2), 218-222

CODEN: JNREDK; ISSN: 0360-4012

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have determined the effects of the calpain inhibitors AK275 and AK295 upon purified m-calpain and calcium-mediated degradation of neurofilament protein (NFP) in rat spinal cord in vitro. After incubation, the soluble radioactivity and/or extent of myelin basic protein (MBP) or NFP degradation was determined Fifty percent of caseinolytic activity was

inhibited by both inhibitors at 0.6  $\mu$ M concentration, while more than 90% inhibition was seen at 1.6  $\mu$ M. In contrast, 37% and 64% inhibition of MBP degradation was seen with AK295 and AK275, resp., at 10  $\mu$ M concentration

The

extent of NFP degradation in spinal cord was quantified from immunoblot enhanced chemiluminescence. The calcium-mediated breakdown of NFP was inhibited by both AK275 and AK295, and the inhibition was dose-dependent. A 50% inhibition of NFP degradation was seen with AK295 at 10 pM and was almost completely inhibited at 25-50  $\mu$ M. AK295 was slightly more potent than AK275. These studies suggest that these potent calpain inhibitors may be used therapeutically to provide neuroprotection in vivo in exptl. central nervous system trauma and ischemia.

IT 160399-35-9, AK 295

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

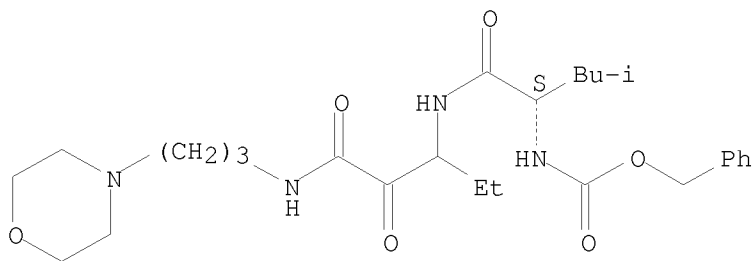
(AK 295; new inhibitors of calpain prevent degradation of cytoskeletal and myelin proteins in rat spinal cord in vitro)

RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

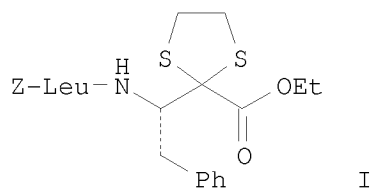
Currently available stereo shown.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1997:208120 CAPLUS  
 DOCUMENT NUMBER: 126:264363  
 ORIGINAL REFERENCE NO.: 126:51209a,51212a  
 TITLE: Preparation of peptidyl ketoamides as serine protease and cysteine protease inhibitors  
 INVENTOR(S): Powers, James C.  
 PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA  
 SOURCE: U.S., 17 pp., Cont. of U. S. Ser. No.247,081.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5610297	A	19970311	US 1995-539946	19951006 <--
PRIORITY APPLN. INFO.:			US 1991-815073	B1 19911227 <--
			US 1993-118997	B1 19930909 <--
			US 1994-247081	B1 19940520 <--
OTHER SOURCE(S):	MARPAT 126:264363			
GI				



AB A novel class of peptide  $\alpha$ -ketoamides M1-AA-NHCHR2CO-CONR3R4, M1-AA2-AA1-CONR3R4, and M1-(AA)n-NR3R4 [M1 = H, H2NCO, H2NCS, H2NSO2, XNHCO, X2NCO, XNHCS, X2NCS, XNHSO2, X2NSO2XCO, CXCS, XSO2, XO2C, XOCS; X = C1-10 alkyl or C1-10 fluoroalkyl optionally substituted with halogen, CO2H, OH, CN, NO2, NH2, C1-10 alkoxy, C1-10 alkylamino, C2-12 dialkylamino, C1-10 alkoxycarbonyl, C1-10 alkoxycarbonylamino, C1-10 alkylthio; 1-adamantyl; 9-fluorenyl; Ph, naphthyl, C1-10 alkylphenyl, or C1-10 alkylphenoxy substituted with 0-3 halogen, C1-10 alkyl, C1-10 perfluoroalkyl, C1-10 alkoxy, NO2, CN, OH, CO2H, amino, C1-10 alkylamino, C2-12 dialkylamino, C1-10 acyl, C1-10 alkoxycarbonyl, C1-10 alkylthio; AA, AA1, AA2 = independently side chain blocked or unblocked amino acid with D-, L-, or no configuration; R2 = C1-8 (un)branched alkyl, C1-8

(un)branched cycloalkyl, C1-8 (un)branched fluoroalkyl; R3, R4 = independently H, C1-20 alkyl, C3-30 cycloalkyl, C1-20 alkyl with attached Ph group containing 0-3 substituents as above; C3-20 cycloalkyl with attached Ph group containing 0-1 substituents as above; etc.; n = 1, 3, 4] were prepared as compds. useful for selectively inhibiting serine proteases, selectively inhibiting cysteine proteases, generally inhibiting all serine proteases, and generally inhibiting all cysteine proteases. Thus, condensation of protected peptidyl ketoester I (Z = PhCH2O2C) (prepared in 3 steps from Z-Phe-Leu-OH, Et oxalyl chloride, and 1,2-ethanedithiol) with alkylamines RNH2 (R = Et, Pr, Bu, CH2CHMe2, CH2Ph, CH2CH2Ph) gave peptidyl ketoamides Z-Phe-Leu-CONHR (II). Peptidyl ketoamides II inhibited chymotrypsin with  $K_i = 8-73 \mu\text{M}$ , and had half-lives in liver and plasma of  $>60$ .

IT 144231-72-1P 144231-73-2P 144231-74-3P  
 144231-75-4P 144231-76-5P 144231-77-6P  
 144231-78-7P 144231-79-8P 144231-80-1P  
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 144863-87-6P

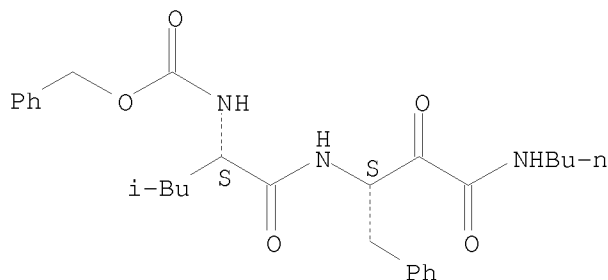
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptidyl ketoamides as serine protease and cysteine protease inhibitors)

RN 144231-72-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

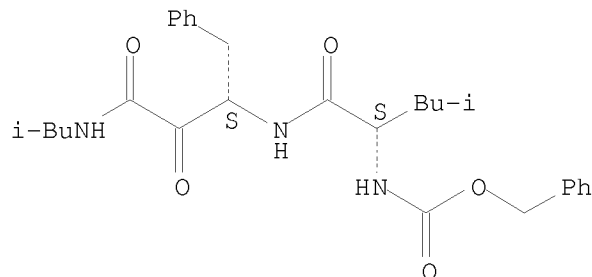
Absolute stereochemistry.



RN 144231-73-2 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-[(2-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

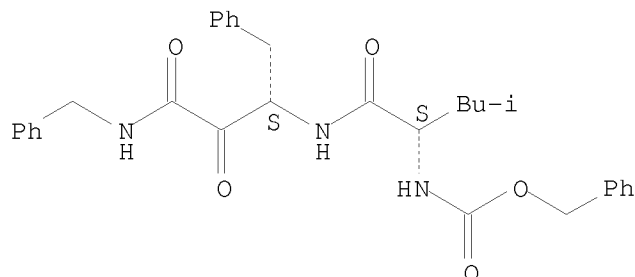
Absolute stereochemistry.



RN 144231-74-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

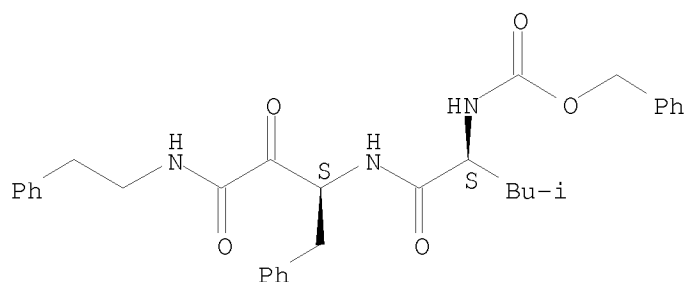
Absolute stereochemistry.



RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

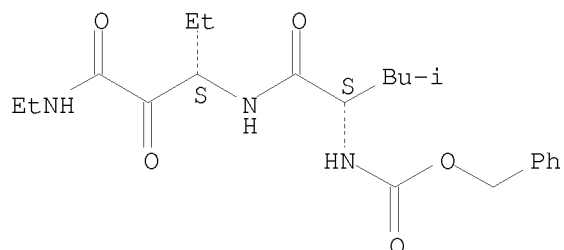
Absolute stereochemistry.



RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

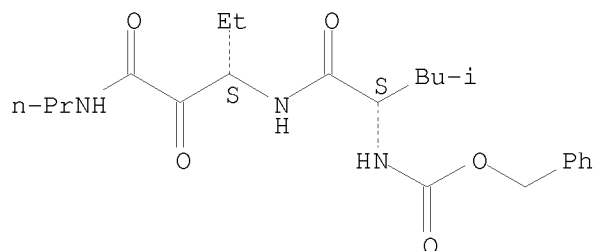
Absolute stereochemistry.



RN 144231-77-6 CAPLUS

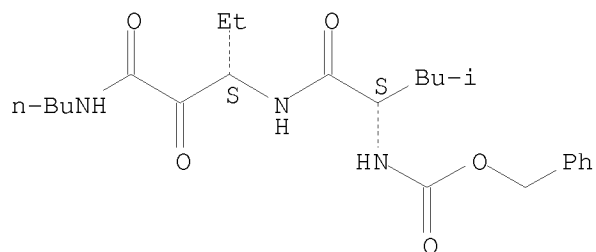
CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



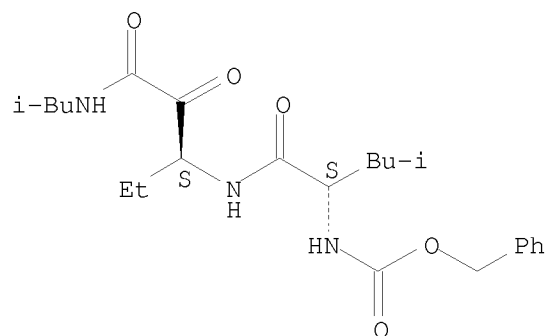
RN 144231-78-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144231-79-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

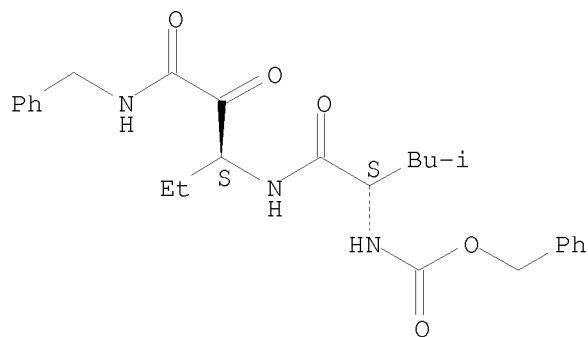
Absolute stereochemistry.



RN 144231-80-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

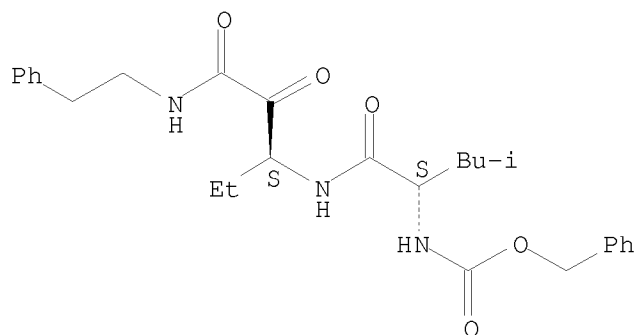




RN 144231-81-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

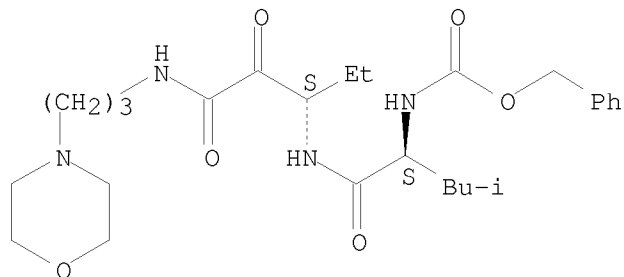
Absolute stereochemistry.



RN 144231-82-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

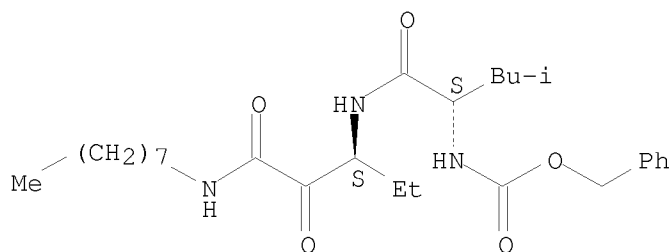
Absolute stereochemistry.



RN 144231-83-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

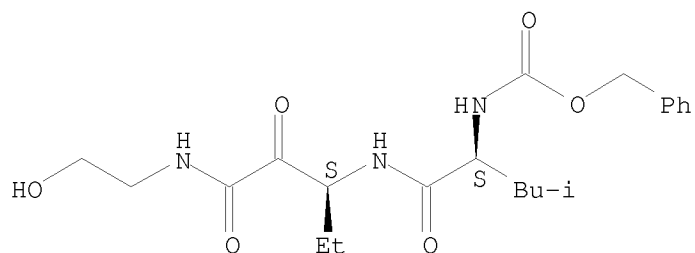
Absolute stereochemistry.



RN 144231-84-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

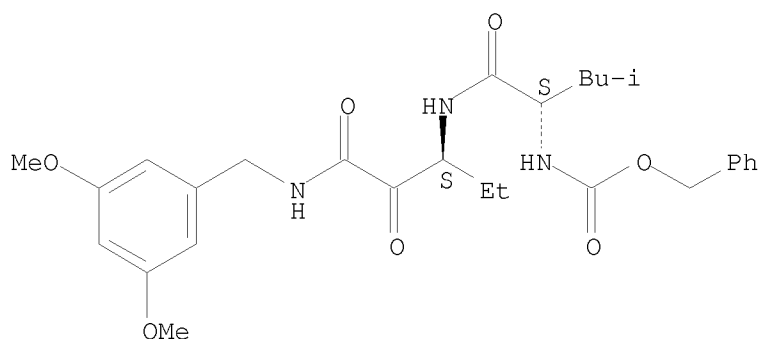
Absolute stereochemistry.



RN 144231-85-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

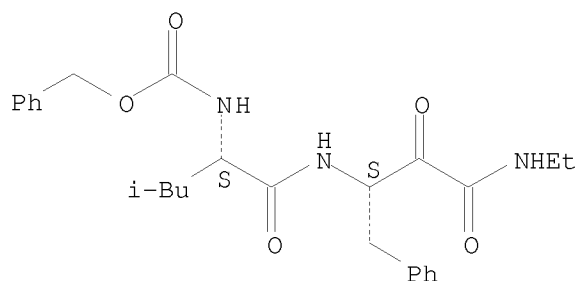
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

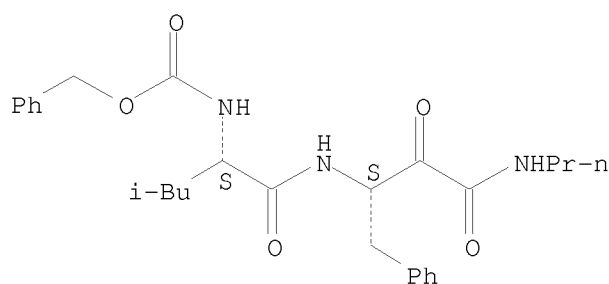
Absolute stereochemistry.



RN 144248-94-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

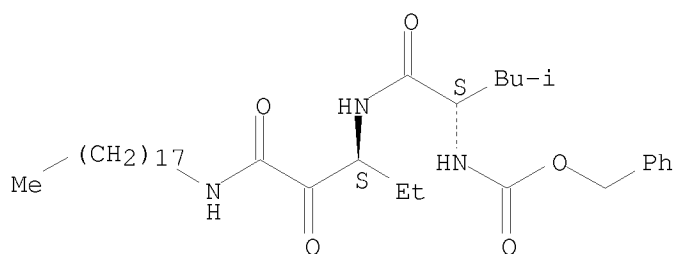
Absolute stereochemistry.



RN 144248-95-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octadecylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

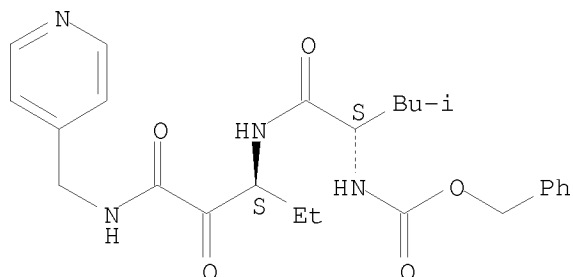
Absolute stereochemistry.



RN 144248-96-4 CAPLUS

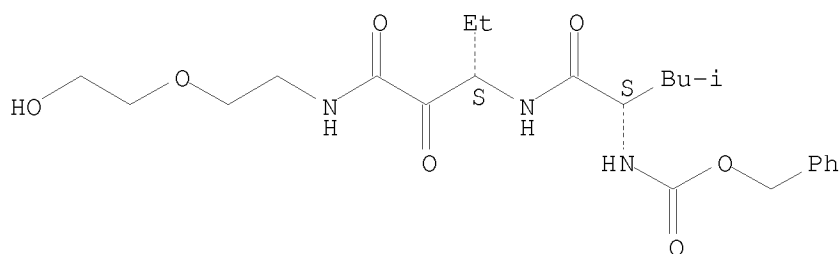
CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144863-87-6 CAPLUS  
 CN 12-Oxa-2,5,9-triazatetradecanoic acid,  
 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester,  
 (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1996:544115 CAPLUS  
 DOCUMENT NUMBER: 125:237576  
 ORIGINAL REFERENCE NO.: 125:44093a,44096a  
 TITLE: Novel Peptidyl  $\alpha$ -Keto Amide Inhibitors of  
 Calpains and Other Cysteine Proteases  
 AUTHOR(S): Li, Zhaozhao; Ortega-Vilain, Anne-Cecile; Patil,  
 Girish S.; Chu, Der-Lun; Foreman, J. E.; Eveleth,  
 David D.; Powers, James C.  
 CORPORATE SOURCE: School of Chemistry and Biochemistry, Georgia  
 Institute of Technology, Atlanta, GA, 30332-0400, USA  
 SOURCE: Journal of Medicinal Chemistry (1996),  
 39(20), 4089-4098  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A series of new dipeptidyl  $\alpha$ -keto amides of the general structure  
 R1-L-Leu-D,L-AA-CONH-R2 were synthesized and evaluated as inhibitors for  
 the cysteine proteases calpain I, calpain II, and cathepsin B. They  
 combine 10 different N-protecting groups (R1), 3 amino acids residues in  
 P1 (AA), and 44 distinct substituents on the  $\alpha$ -keto amide nitrogen  
 (R2). In general, calpain II was more sensitive to these inhibitors than  
 calpain I, with a large number of inhibitors displaying dissociation consts.

(Ki) in the 10-100 nM range. Calpain I was also effectively inhibited, but  
 very low Ki values were observed with a smaller number of inhibitors than with  
 calpain II. Cathepsin B was weakly inhibited by most compds. in this  
 study. The best inhibitors for calpain II were  
 Z-Leu-Abu-CONH-CH2-CHOH-C6H5 (Ki = 15 nM), Z-Leu-Abu-CONH-CH2-2-pyridyl

( $K_i = 17$  nM), and Z-Leu-Abu-CONH-CH<sub>2</sub>-C<sub>6</sub>H<sub>3</sub>(3,5(OMe)<sub>2</sub>) ( $K_i = 22$  nM). The best calpain I inhibitor in this study was Z-Leu-Nva-CONH-CH<sub>2</sub>-2-pyridyl ( $K_i = 19$  nM). The peptide  $\alpha$ -keto amide Z-Leu-Abu-CONH-(CH<sub>2</sub>)<sub>2</sub>-3-indolyl was the best inhibitor for cathepsin B ( $K_i = 31$  nM). Some compds. acted as specific calpain inhibitors, with comparable activity on both calpains I and II and a lack of activity on cathepsin B. Others were specific inhibitors for calpain I (e.g., 73) or calpain II. Such inhibitors may be useful in elucidating the physiol. and pathol. events involving these proteases and may become possible therapeutic agents.

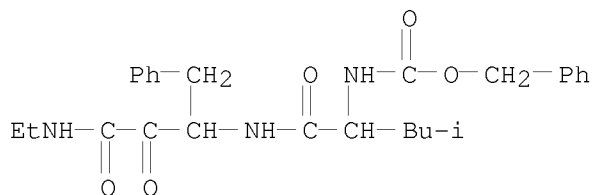
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 181963-37-1P 181963-38-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of novel peptidyl  $\alpha$ -keto amide inhibitors of calpains and other cysteine proteases)

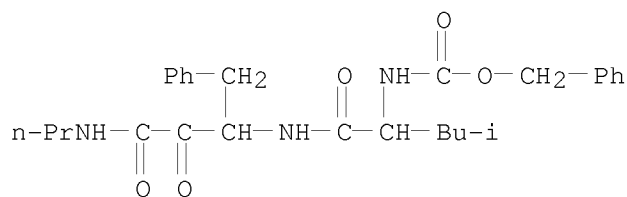
RN 145731-36-8 CAPLUS

CN Carbamic acid, [1-[[[3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



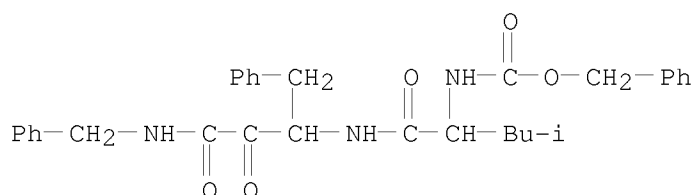
RN 145731-38-0 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



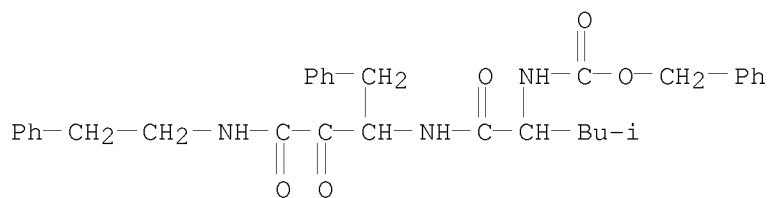
RN 145731-41-5 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



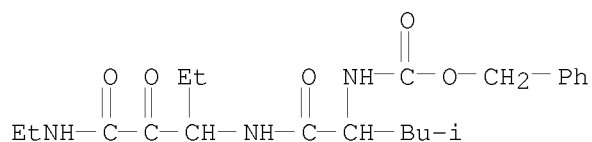
RN 145731-42-6 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



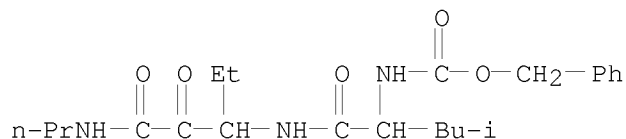
RN 145731-43-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



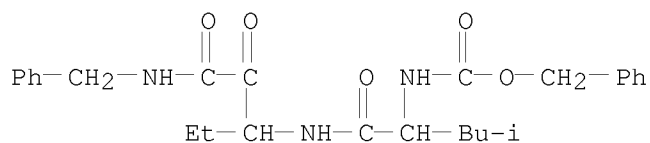
RN 145731-44-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



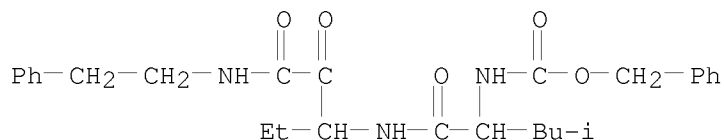
RN 145731-47-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



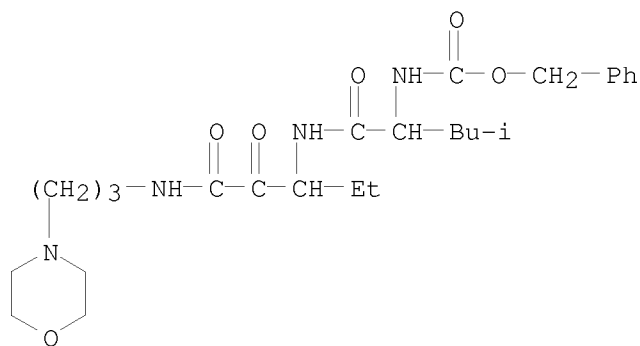
RN 145731-48-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



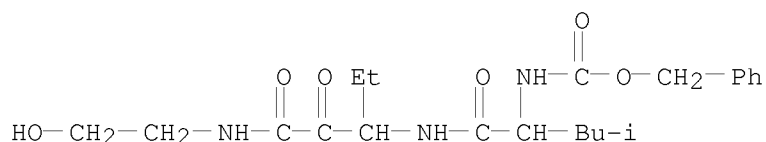
RN 145731-49-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



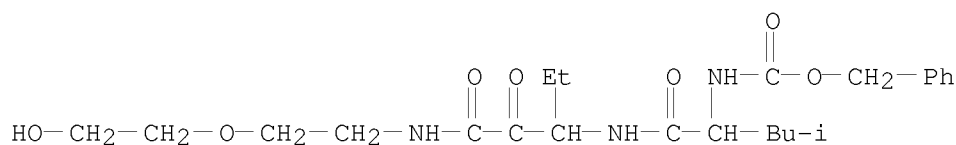
RN 145731-51-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



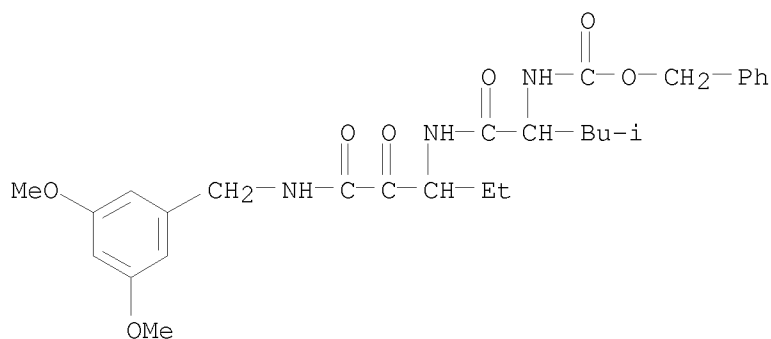
RN 145731-52-8 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid,  
6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester  
(CA INDEX NAME)



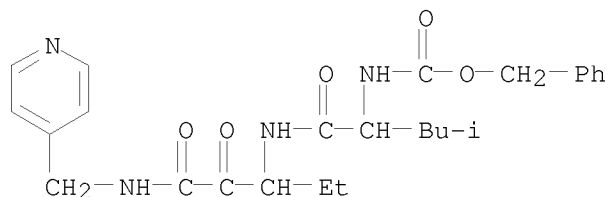
RN 145731-54-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 145731-55-1 CAPLUS

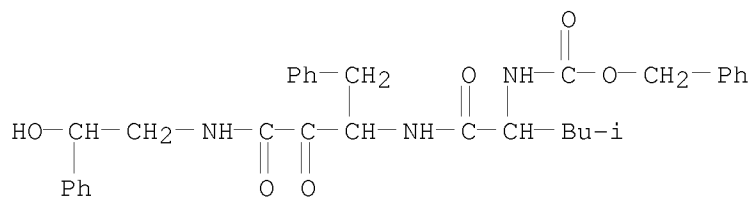
CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-23-1 CAPLUS

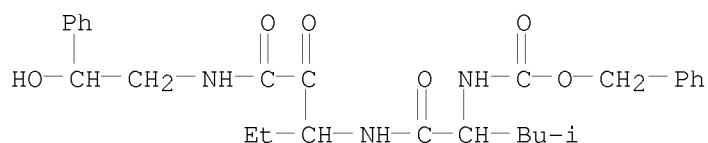
CN Carbamic acid, [1-[[[3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)





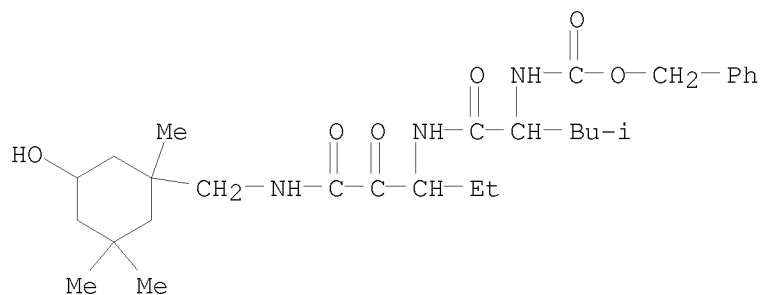
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CN Carbamic acid, [1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



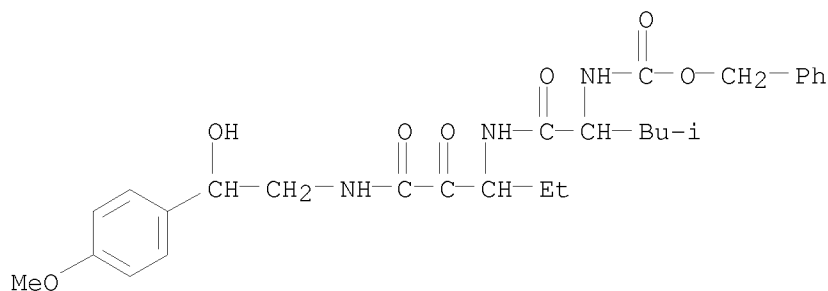
RN 153370-37-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(5-hydroxy-1,3,3-trimethylcyclohexyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



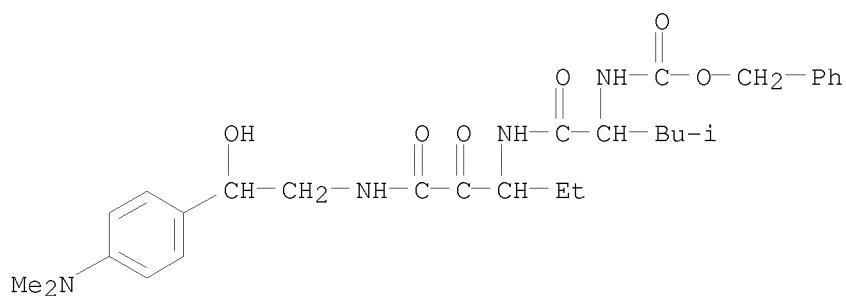
RN 153370-43-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



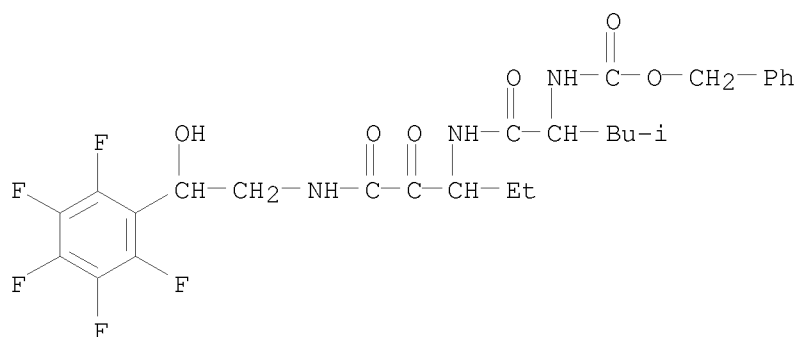
RN 153370-45-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



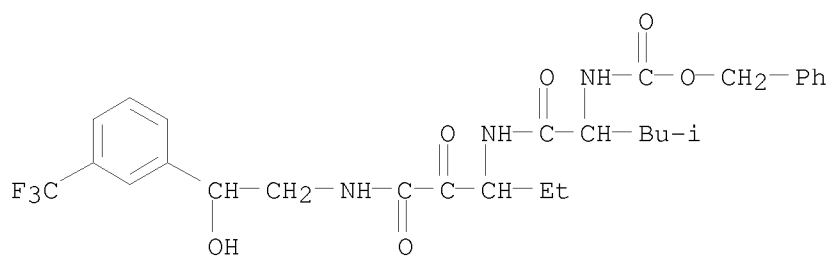
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CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



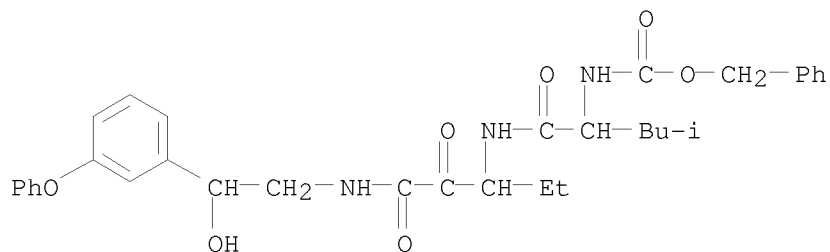
RN 153370-47-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



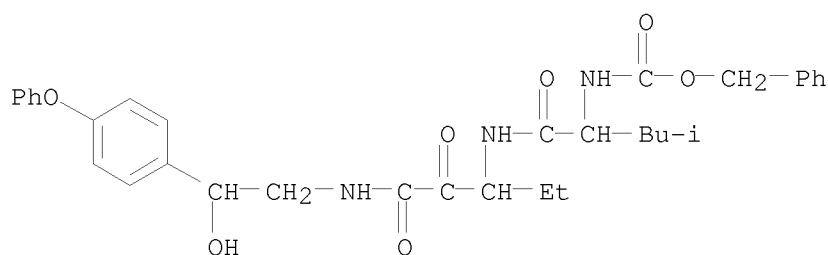
RN 153370-48-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



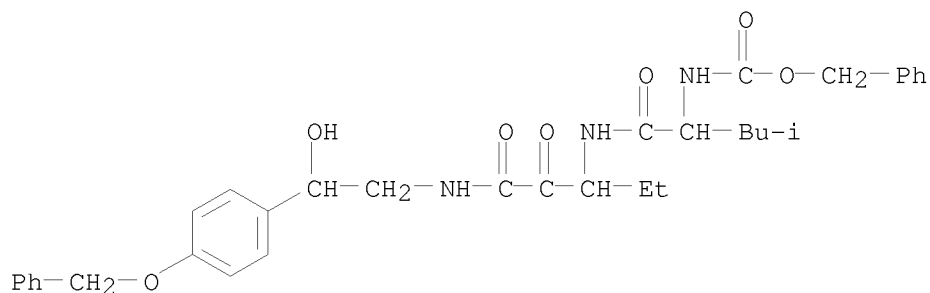
RN 153370-49-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



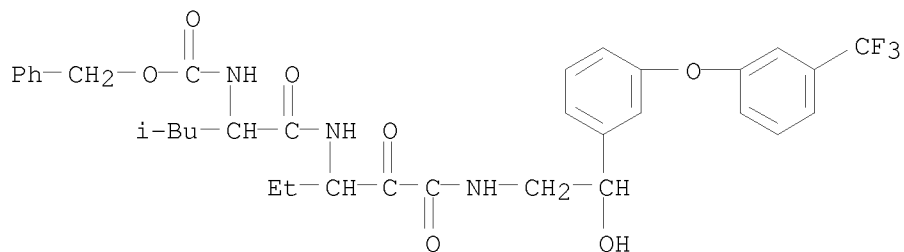
RN 153370-50-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



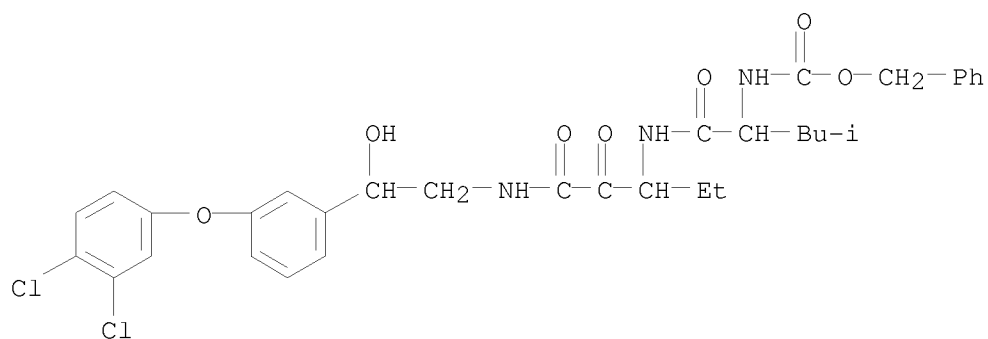
RN 153370-51-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



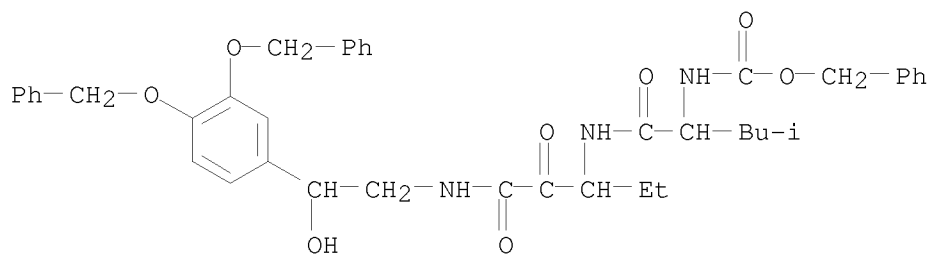
RN 153370-52-6 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



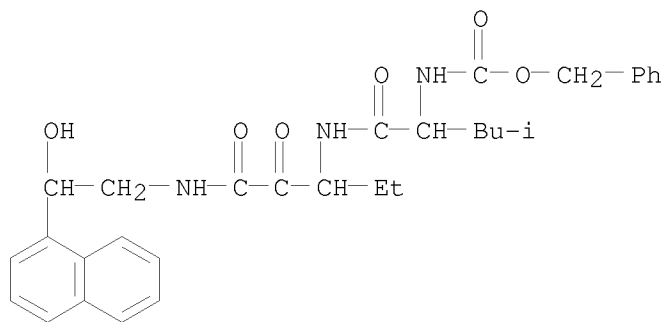
RN 153370-53-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



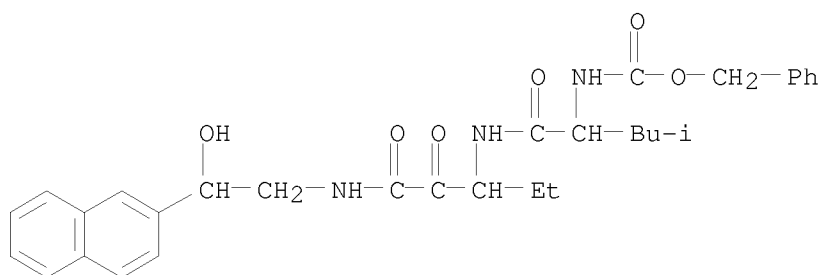
RN 153370-54-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(1-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



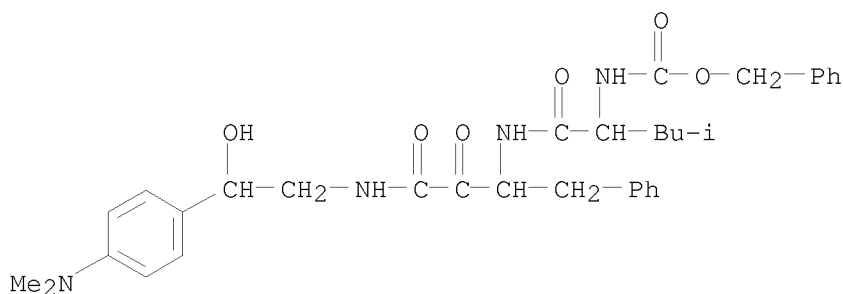
RN 153370-55-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(2-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



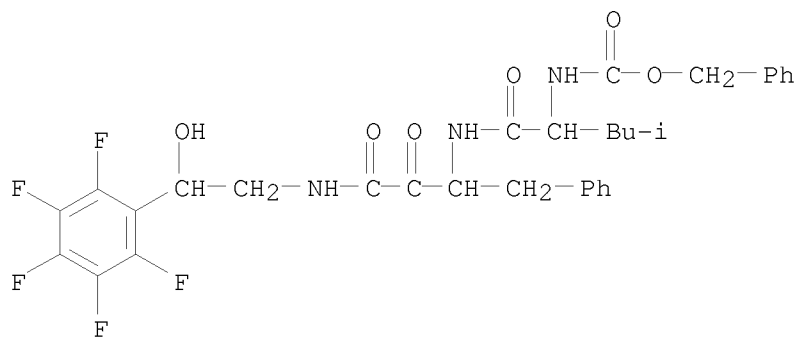
RN 153370-56-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



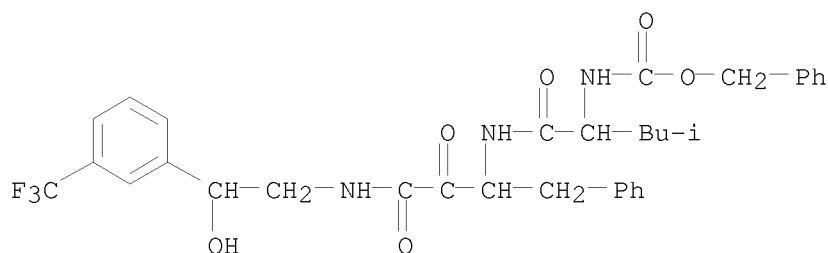
RN 153370-57-1 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



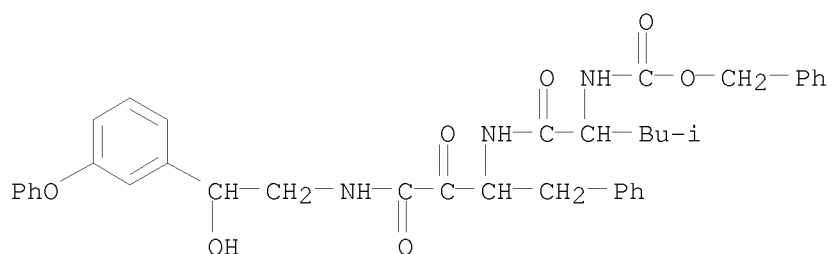
RN 153370-58-2 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



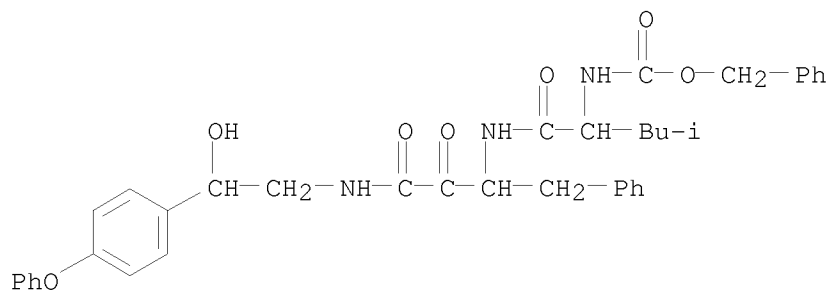
RN 153370-59-3 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



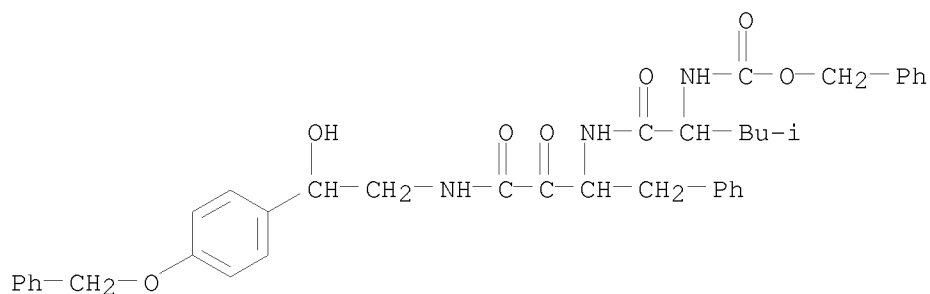
RN 153370-60-6 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



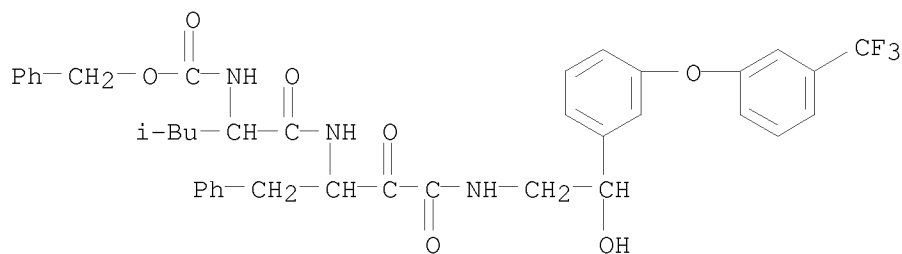
RN 153370-61-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



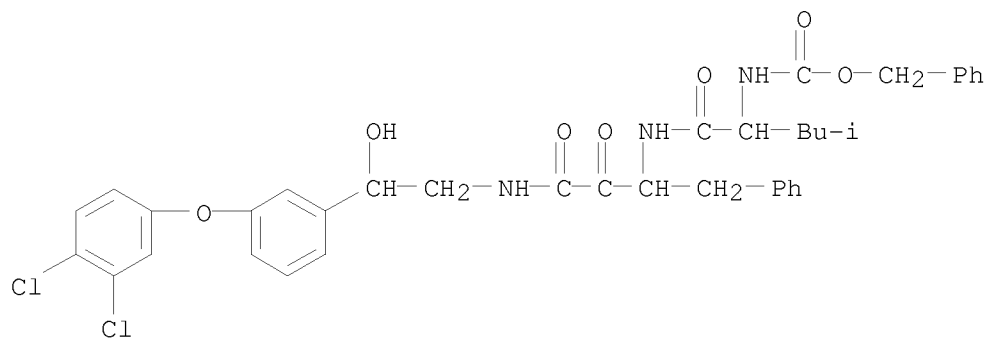
RN 153370-62-8 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



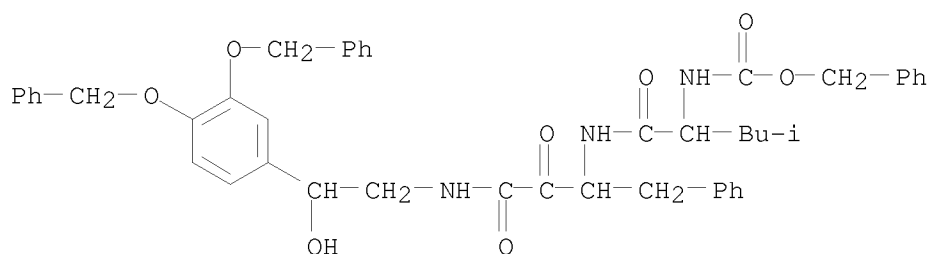
RN 153370-63-9 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



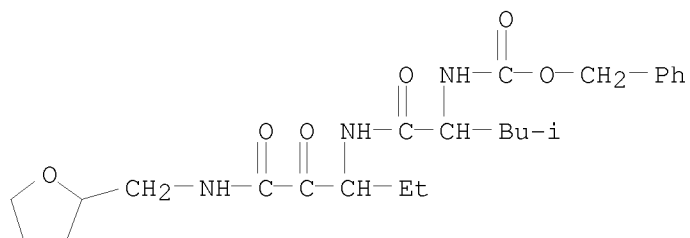
RN 153370-64-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



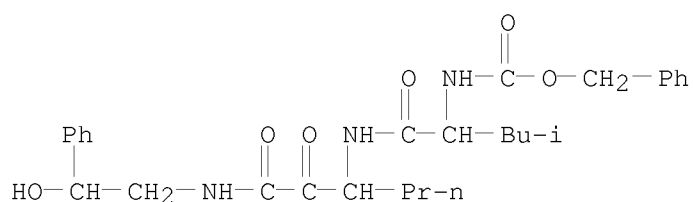
RN 153370-66-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[tetrahydro-2-furanyl]methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



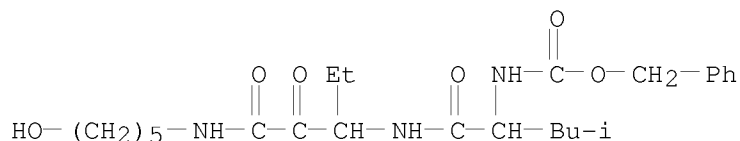
RN 153370-89-9 CAPLUS

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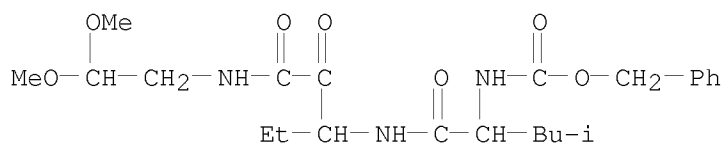




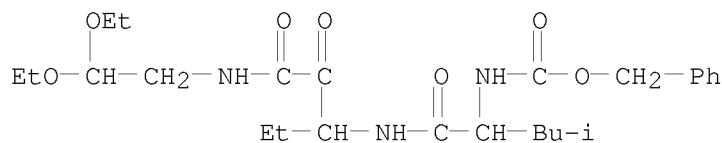
RN 178675-31-5 CAPLUS  
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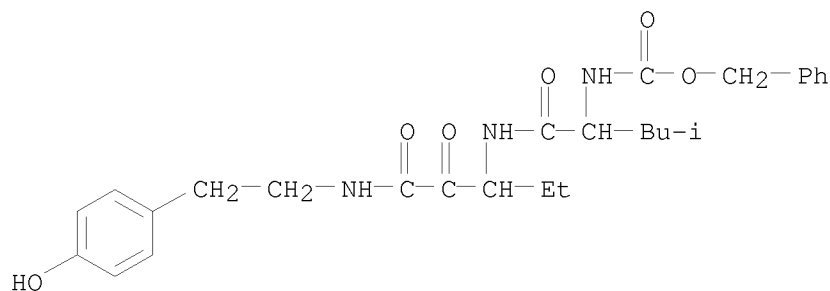
RN 178675-32-6 CAPLUS  
 CN 12-Oxa-2,5,9-triazatridecanoic acid, 6-ethyl-11-methoxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester (CA INDEX NAME)



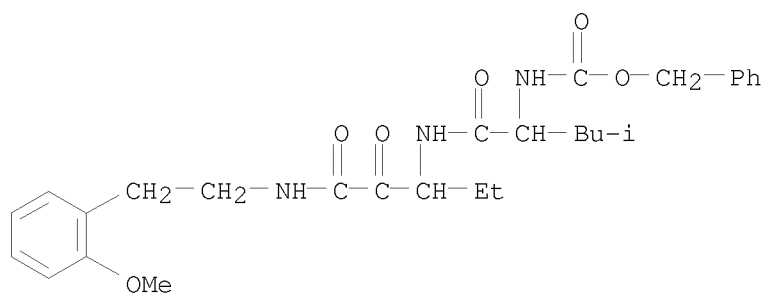
RN 178675-33-7 CAPLUS  
 CN 12-Oxa-2,5,9-triazatetradecanoic acid, 11-ethoxy-6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester (CA INDEX NAME)



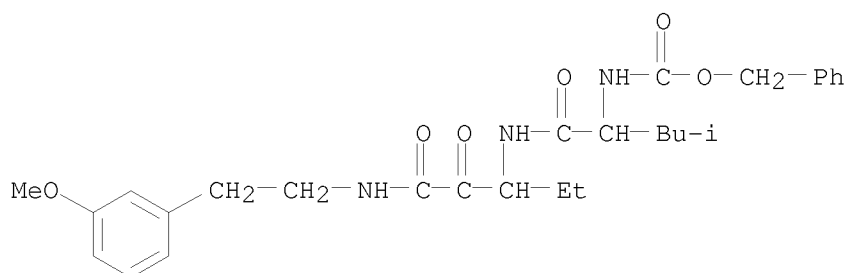
RN 178675-34-8 CAPLUS  
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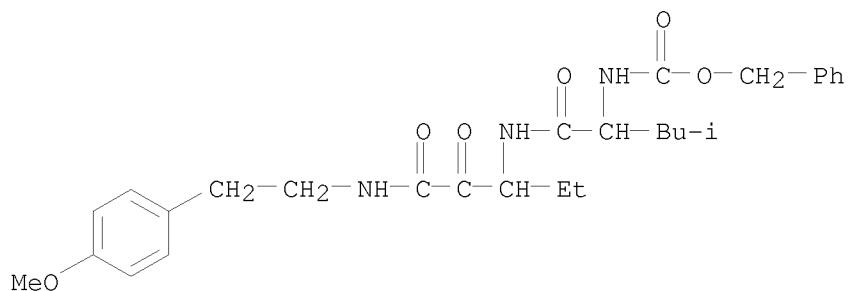
RN 178675-35-9 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(2-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



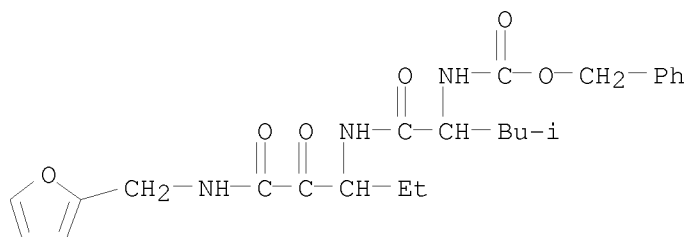
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RN 178675-37-1 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

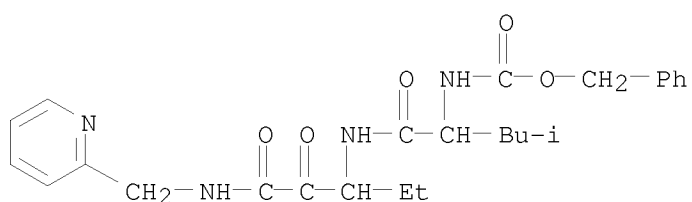


RN 178675-38-2 CAPLUS  
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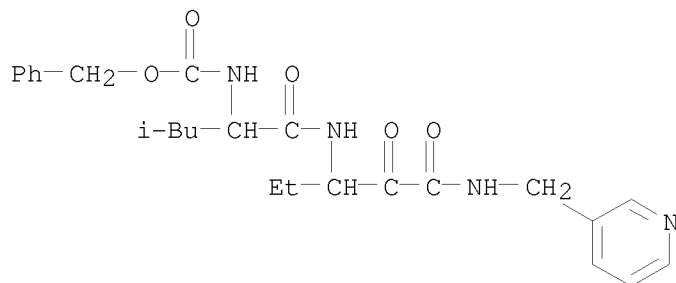
RN 178675-39-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



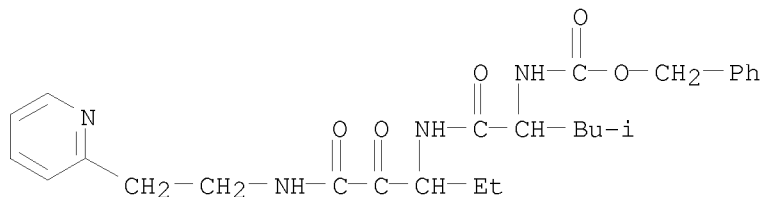
RN 178675-40-6 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(3-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 178675-41-7 CAPLUS

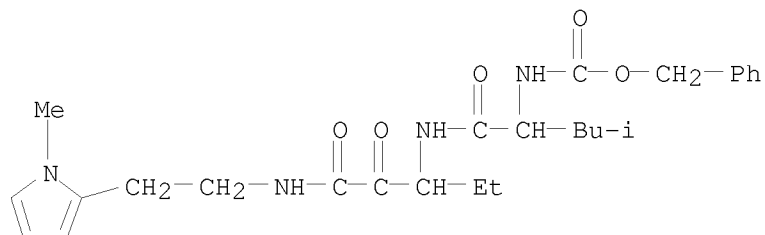
CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2-(2-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 178675-42-8 CAPLUS

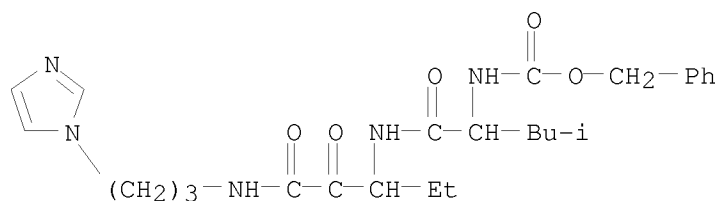
CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(1-methyl-1H-pyrrol-2-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)

(CA INDEX NAME)



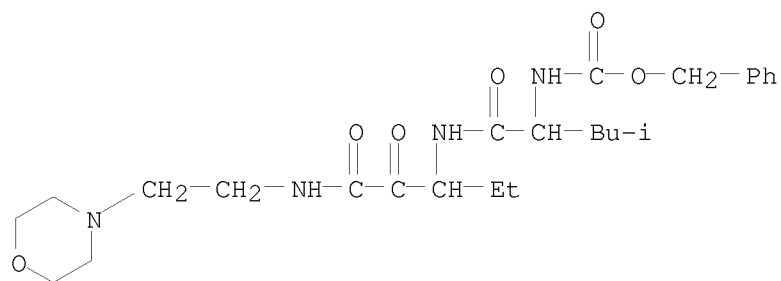
RN 178675-43-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[3-(1H-imidazol-1-yl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



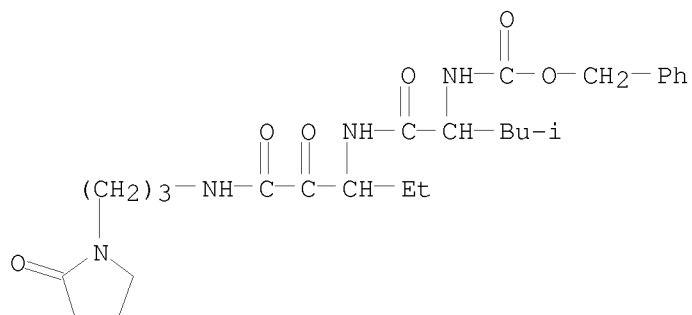
RN 178675-44-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-morpholinyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



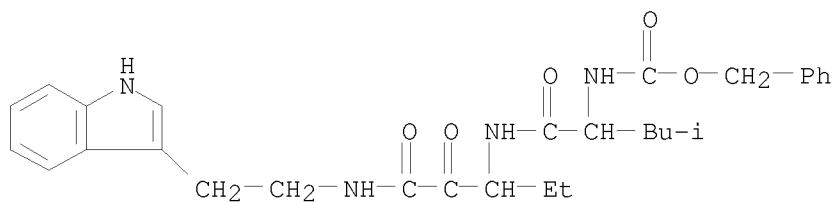
RN 178675-45-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



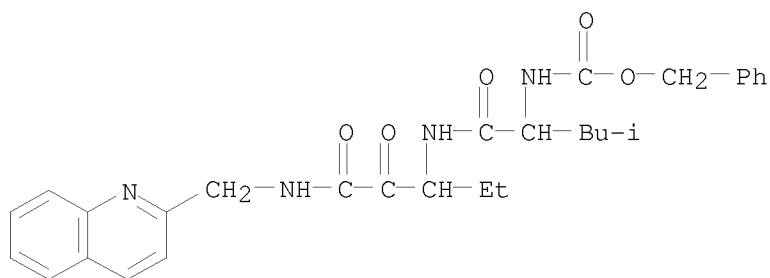
RN 178675-46-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(1H-indol-3-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



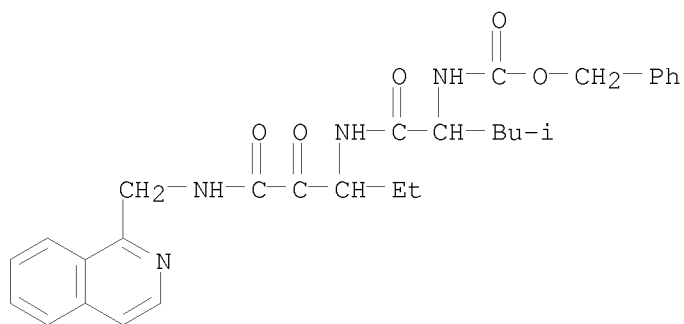
RN 178675-47-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



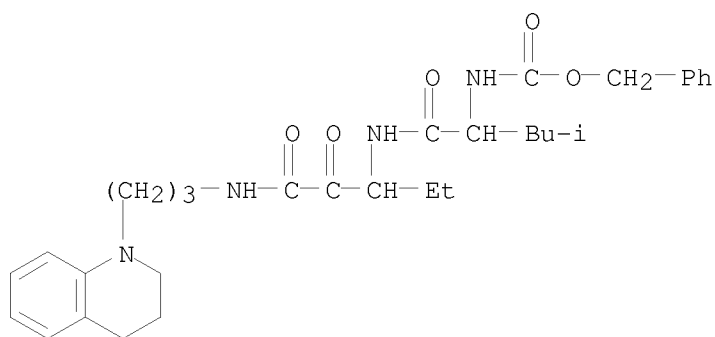
RN 178675-48-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(1-isoquinolinylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



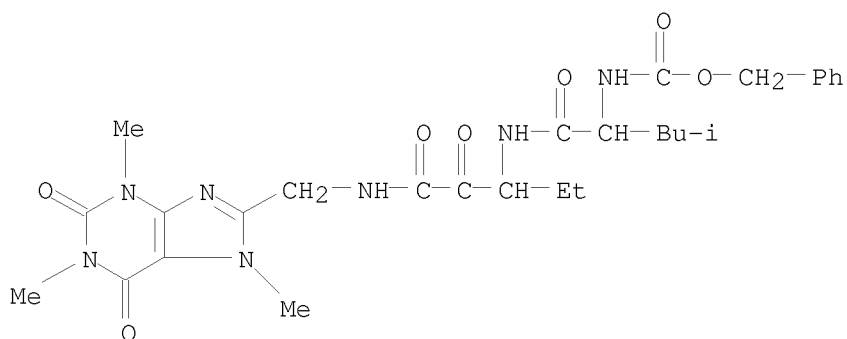
RN 178675-49-5 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



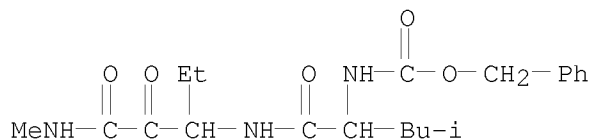
RN 178675-51-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



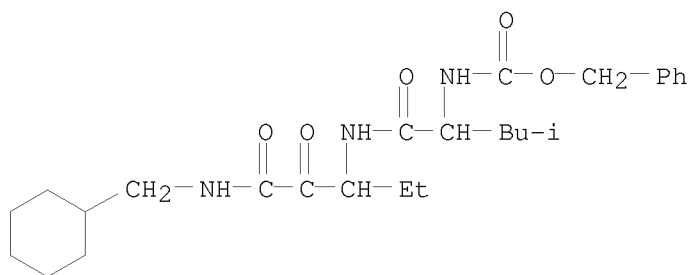
RN 181769-43-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(methylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



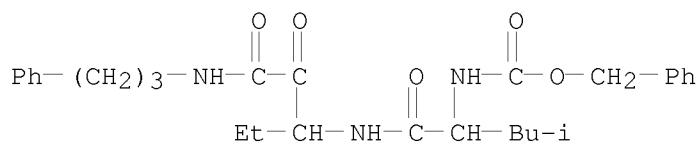
RN 181769-46-0 CAPLUS

CN Carbamic acid, [1-[[[3-[(cyclohexylmethyl)amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



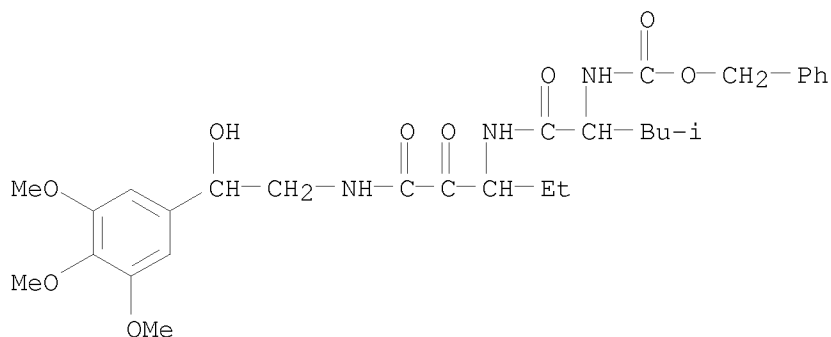
RN 181769-47-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(3-phenylpropyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 181769-48-2 CAPLUS

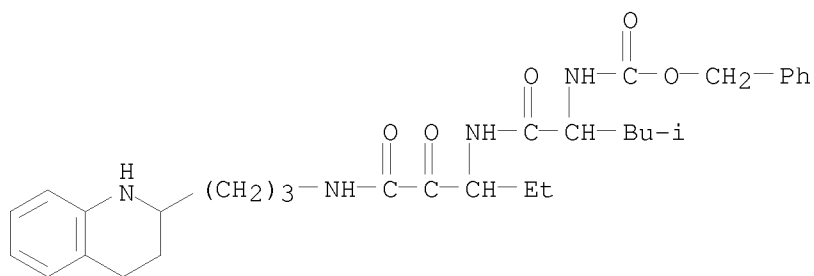
CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(3,4,5-trimethoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 181769-49-3 CAPLUS

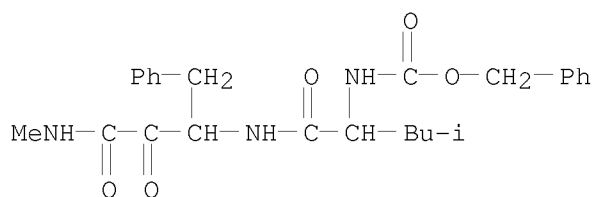
CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[3-(1,2,3,4-tetrahydro-2-quinolinyl)propyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-,

phenylmethyl ester (9CI) (CA INDEX NAME)



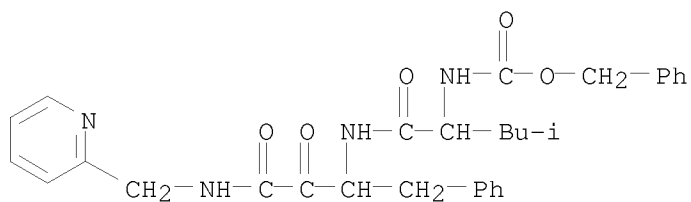
RN 181769-50-6 CAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-(methylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



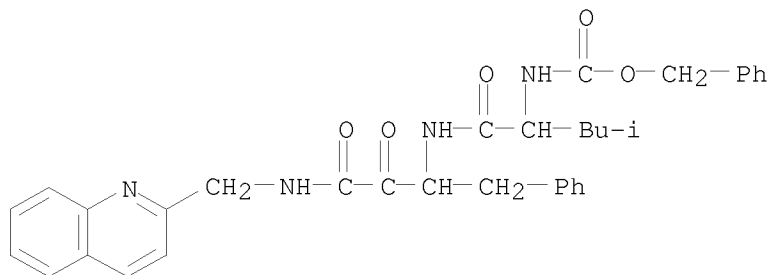
RN 181769-52-8 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



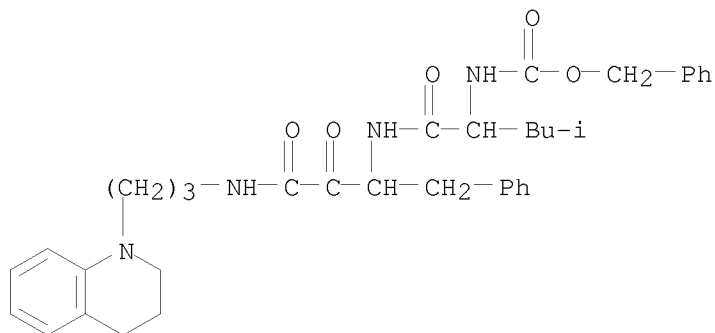
RN 181769-53-9 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

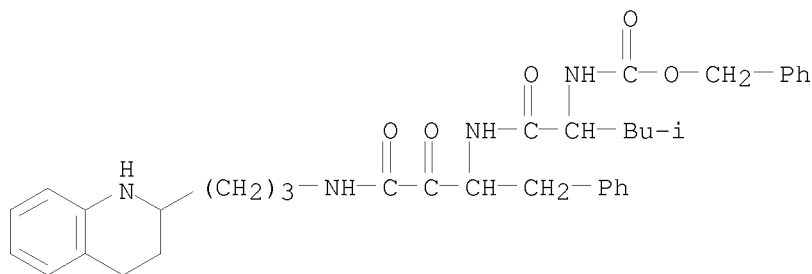




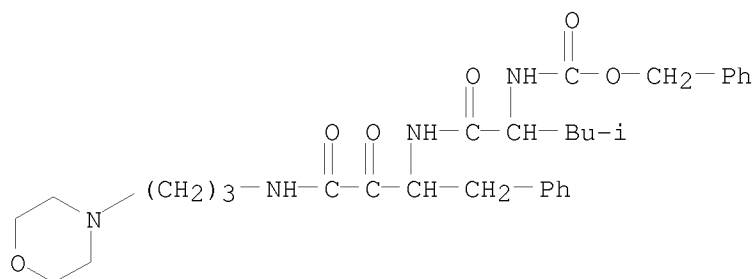
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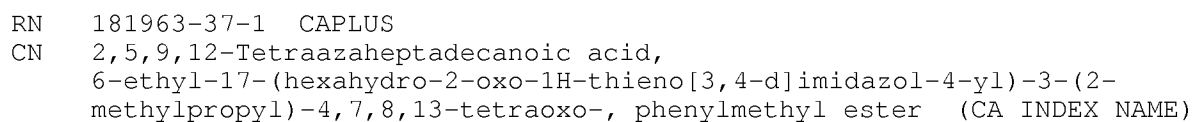
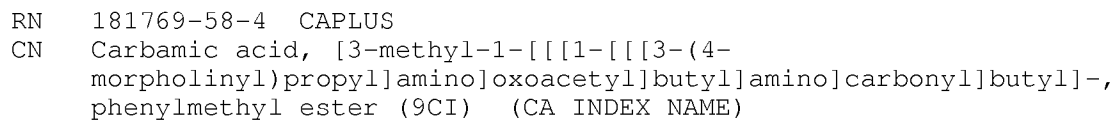
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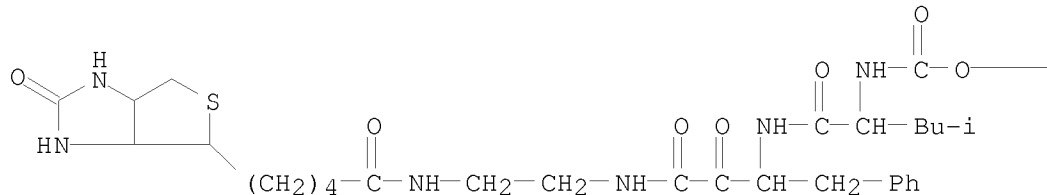
RN 181769-56-2 CAPLUS  
 CN Carbamic acid, [3-methyl-1-[[[3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 181769-57-3 CAPLUS  
 CN Carbamic acid, [3-methyl-1-[[[1-[oxo[(2-pyridinylmethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

CC1(C)SCC2C1NC(=O)N2C(=O)CCCC(=O)NCC(=O)NCC(=O)NCC(=O)NCC(=O)NCC(=O)OCCCC
$$-\text{CH}_2-\text{Ph}$$

RN	181963-38-2	CAPLUS
CN	2,5,9,12-Tetraazaheptadecanoic acid, 17-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-3-(2-methylpropyl)- 4,7,8,13-tetraoxo-6-(phenylmethyl)-, phenylmethyl ester (CA INDEX NAME)	



—CH<sub>2</sub>—Ph

L10 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:476813 CAPLUS

DOCUMENT NUMBER: 125:143327

ORIGINAL REFERENCE NO.: 125:26853a, 26856a

TITLE: Preparation of  $\alpha$ -ketoamide derivatives as cathepsin L inhibitors.

INVENTOR(S): Sohda, Takashi; Fujisawa, Yukio; Yasuma, Tsuneo; Mizoguchi, Junji

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9616079	A2	19960530	WO 1995-JP2389	19951124 <--
WO 9616079	A3	19960912		
W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 08208462	A	19960813	JP 1995-304852	19951122 <--
CA 2200964	A1	19960530	CA 1995-2200964	19951124 <--
AU 9539358	A	19960617	AU 1995-39358	19951124 <--
EP 793673	A1	19970910	EP 1995-937173	19951124 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			JP 1994-290132	A 19941124 <--
			WO 1995-JP2389	W 19951124 <--

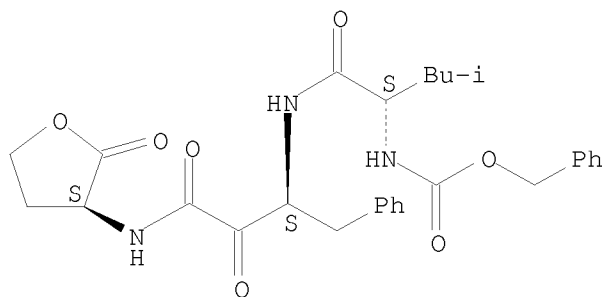
OTHER SOURCE(S): MARPAT 125:143327

AB R4QNHCCHR1COCONR5R6 [Q = bond, 1 or 2 (substituted) amino acid residues R1, R5, R6 = H, (substituted) hydrocarbonyl, heterocyclyl; R4 = acyl, (esterified) carboxyl; R5R6 = atoms to form a ring], were prepared. Thus, N-benzyloxycarbonylisoleucyl-(2R,3S)-3-amino-2-hydroxy-4-phenylbutyric acid benzylamide was stirred with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and pyridinium trifluoroacetate in Me<sub>2</sub>SO/PhMe to give 83%

N-benzyloxycarbonylisoleucyl-(2R,3S)-3-amino-2-oxo-4-phenylbutyric acid.  
The latter inhibited cathepsin L with IC50 = 1.1 + 10-8 M.

IT 179549-96-3P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of  $\alpha$ -ketoamide derivs. as cathepsin L inhibitors)  
RN 179549-96-3 CAPLUS  
CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(tetrahydro-2-oxo-3-furanyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [3S-[3R\*[R\*(R\*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:333049 CAPLUS

DOCUMENT NUMBER: 125:87221

ORIGINAL REFERENCE NO.: 125:16477a,16480a

TITLE: Peptidyl ketoamides as serine and cysteine protease inhibitors

INVENTOR(S): Powers, James C.; Li, Zhaozhao; Patil, Girish S.; Chu, Der-Lun

PATENT ASSIGNEE(S): Georgia Tech Research Corp, USA

SOURCE: U.S., 30 pp., Cont.-in-part of U.S. Ser. No. 948, 454, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5514694	A	19960507	US 1993-83009	19930624 <--
PRIORITY APPLN. INFO.:			US 1992-948454	B2 19920921 <--

OTHER SOURCE(S): MARPAT 125:87221

AB A novel class of peptide  $\alpha$ -ketoamides useful for selectively inhibiting serine proteases, selectively inhibiting cysteine proteases, generally inhibiting all serine proteases, and generally inhibiting all cysteine proteases, has the formula Y-CO-AA2-AA1-CO-NH-X or a pharmaceutically acceptable salt, wherein: Y = e.g., C1-4 alkyl monosubstituted with Ph, C1-4 alkyl disubstituted with Ph, C1-4 alkyl monosubstituted with 1-naphthyl; AA2 is an amino acid with the L configuration, D configuration, or DL configuration at the  $\alpha$ -carbon selected from the group consisting of, e.g., alanine, valine, leucine, isoleucine, proline; AA1 is an amino acid with the L configuration, D configuration, or DL configuration at the  $\alpha$ -carbon selected from the group consisting of, e.g., alanine, 4-chlorophenylalanine, valine,

leucine, isoleucine, proline; X is selected from the group consisting of (a) CH<sub>2</sub>CH(OH)R<sub>1</sub> and (b) (CH<sub>2</sub>)<sub>n</sub>R<sub>3</sub>; R<sub>1</sub> is selected from the group consisting of, e.g., Ph, Ph monosubstituted with J, Ph disubstituted with J, Ph trisubstituted with J, pentafluorophenyl; R<sub>3</sub> is selected from the group consisting of, e.g., 2-furyl, 2-furyl monosubstituted with J, 2-pyridyl, 2-pyridyl monosubstituted with J; n = 1-3; J = e.g., OH, CN, NO<sub>2</sub>. Thus, e.g., the ketone carbonyl of Z-Leu-Abu-CO<sub>2</sub>Et is first protected as a 1,3-dithiolane; amidation with 5-amino-1-pentanol and deprotection afforded Z-Leu-Abu-CONH(CH<sub>2</sub>)<sub>5</sub>OH in 42% yield which exhibited inhibition of cysteine proteases calpain I, calpain II, and cathepsin B with KI = 0.5, 0.051, and 0.28 μM, resp. Z-Leu-Phe-CONHBu exhibited inhibition of serine proteases human leukocyte elastase and cathepsin G with IC<sub>50</sub> = 16 and 68 μM, resp.

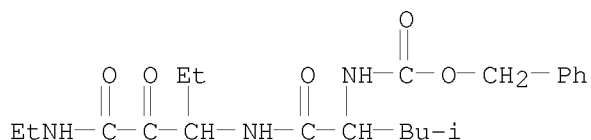
IT 145731-43-7

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)

(peptidyl ketoamides as serine and cysteine protease inhibitors)

RN 145731-43-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



IT 144231-72-1P 144231-73-2P 144231-74-3P  
 144231-75-4P 144248-93-1P 144248-94-2P  
 145731-44-8P 145731-45-9P 145731-46-0P  
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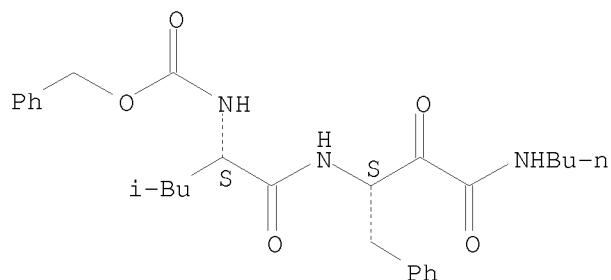
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); PROC (Process); USES (Uses)  
(peptidyl ketoamides as serine and cysteine protease inhibitors)

RN 144231-72-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

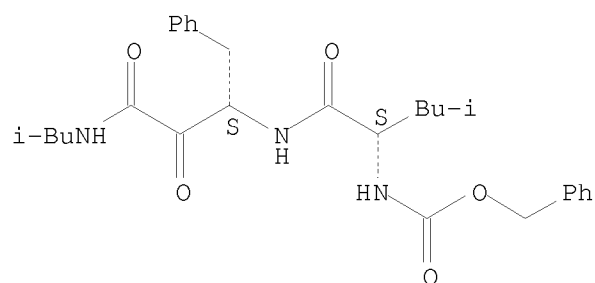
Absolute stereochemistry.



RN 144231-73-2 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-[(2-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

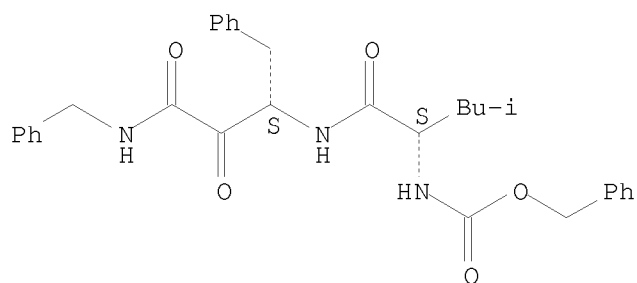
Absolute stereochemistry.



RN 144231-74-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

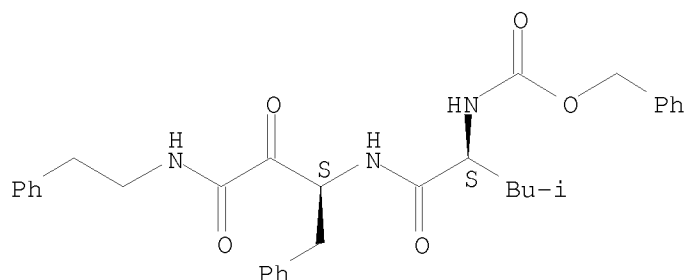


RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-

(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

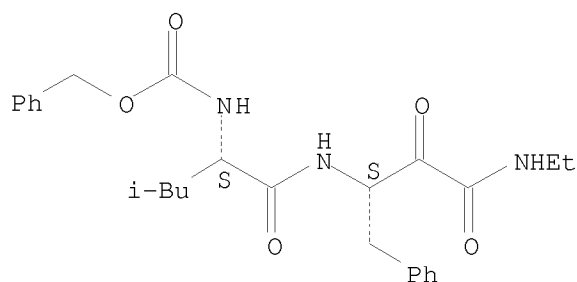
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

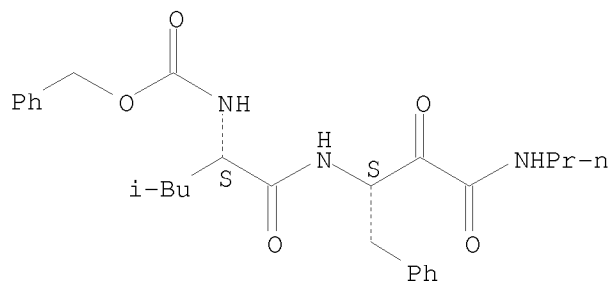
Absolute stereochemistry.



RN 144248-94-2 CAPLUS

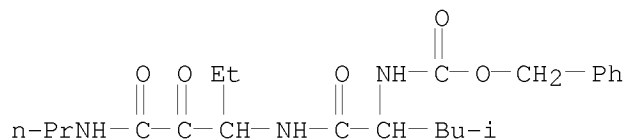
CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



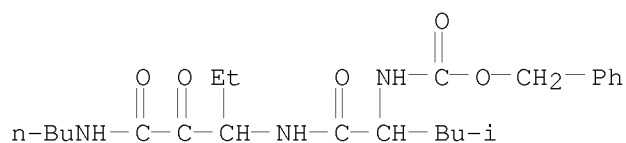
RN 145731-44-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)



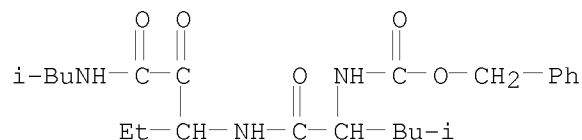
RN 145731-45-9 CAPLUS

CN Carbamic acid, [1-[[[3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



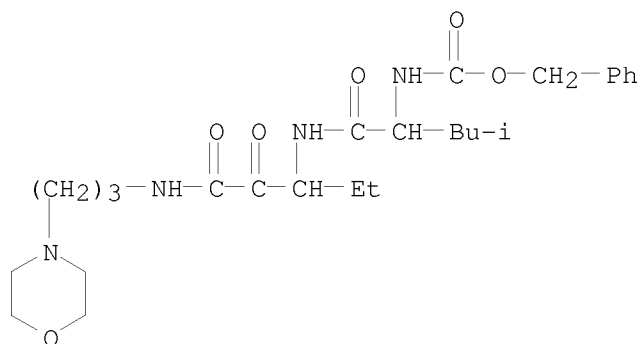
RN 145731-46-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 145731-49-3 CAPLUS

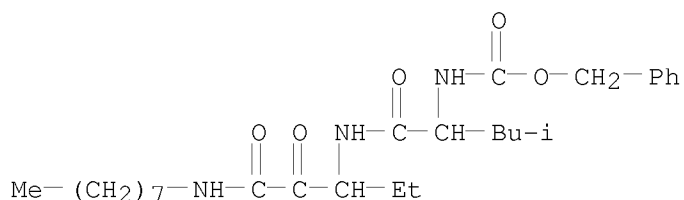
CN Carbamic acid, [1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 145731-50-6 CAPLUS

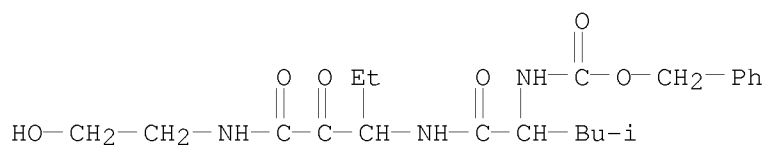
CN Carbamic acid, [1-[[[1-ethyl-3-(octylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)





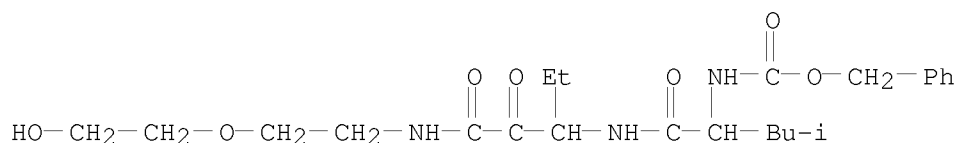
RN 145731-51-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



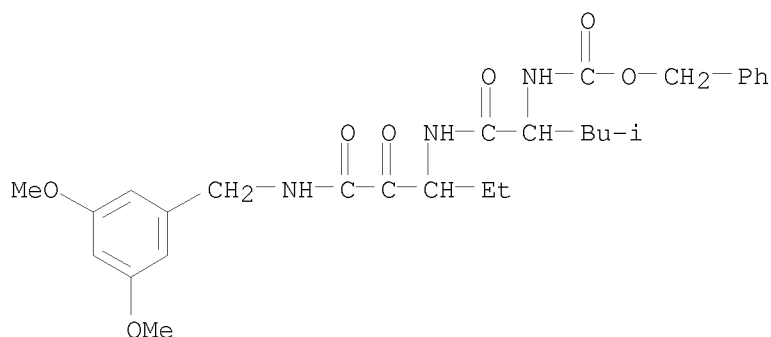
RN 145731-52-8 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid, 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester (CA INDEX NAME)



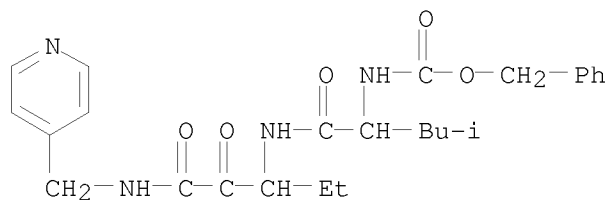
RN 145731-54-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



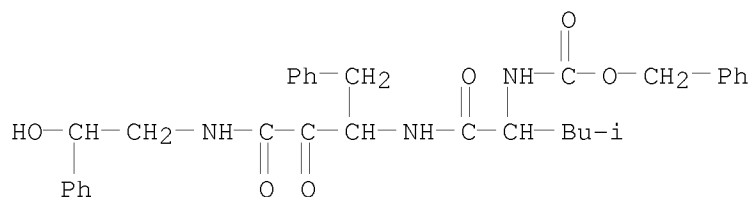
RN 145731-55-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-23-1 CAPLUS

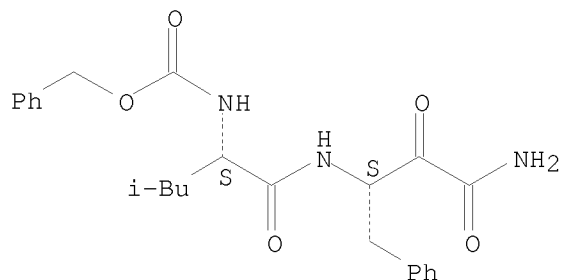
CN Carbamic acid, [1-[[[3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-24-2 CAPLUS

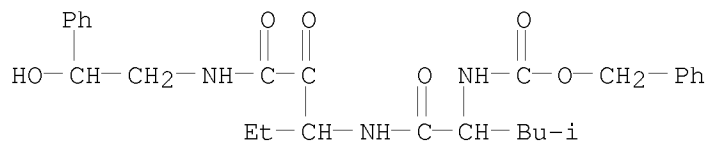
CN Carbamic acid, [1-[[[3-amino-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



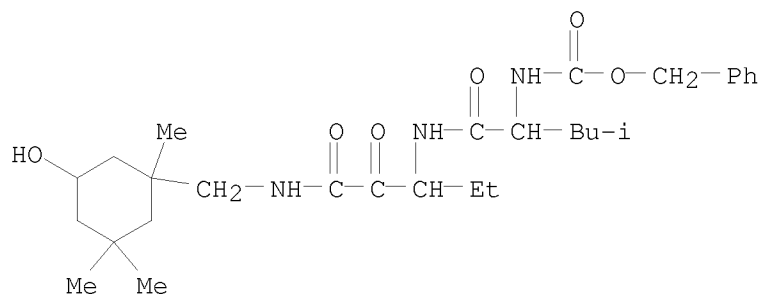
RN 153370-25-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



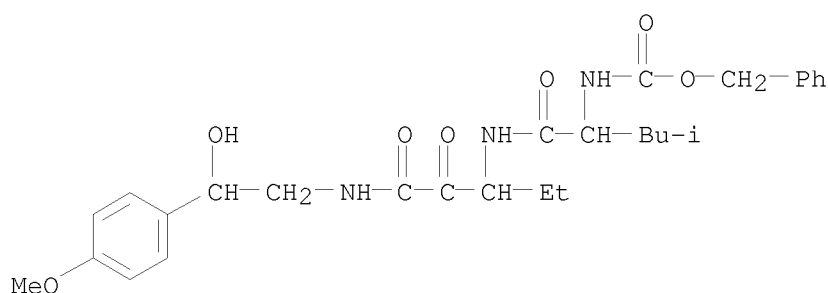
RN 153370-37-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(5-hydroxy-1,3,3-trimethylcyclohexyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



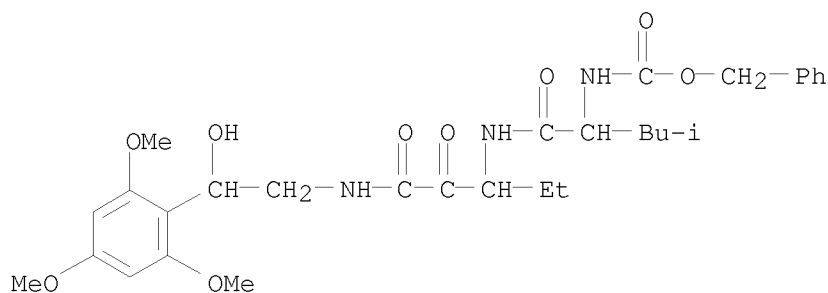
RN 153370-43-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



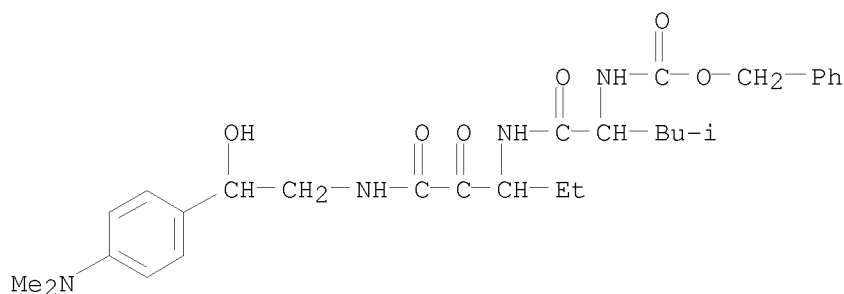
RN 153370-44-6 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(2,4,6-trimethoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



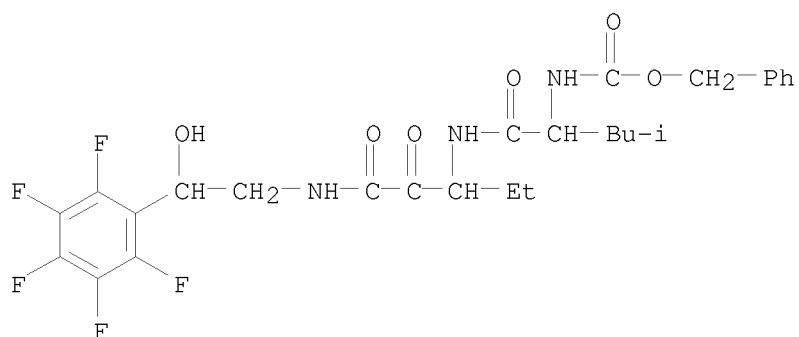
RN 153370-45-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



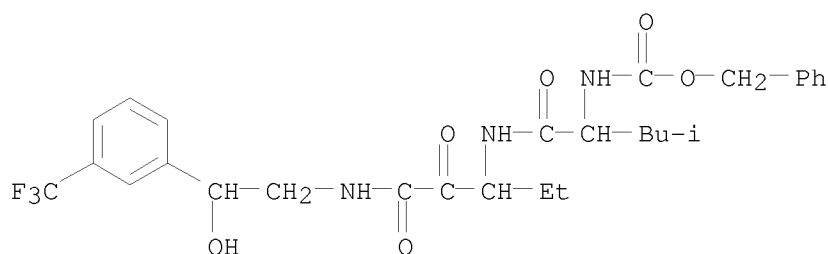
RN 153370-46-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



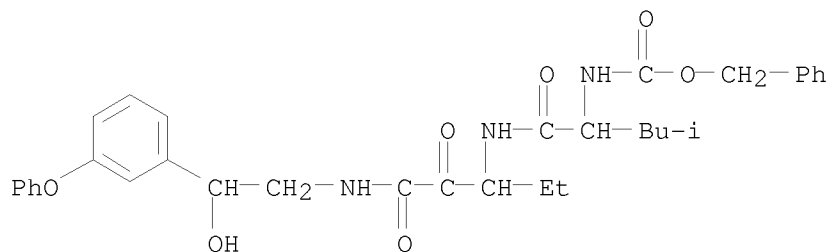
RN 153370-47-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



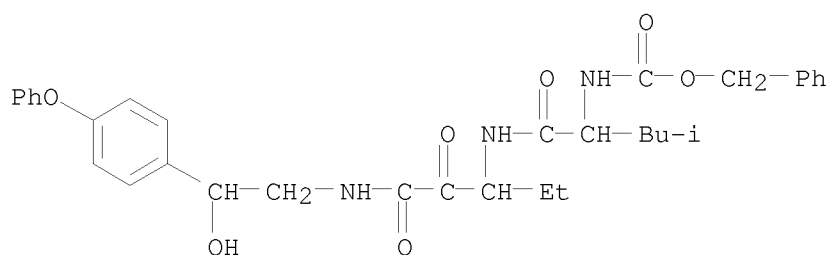
RN 153370-48-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



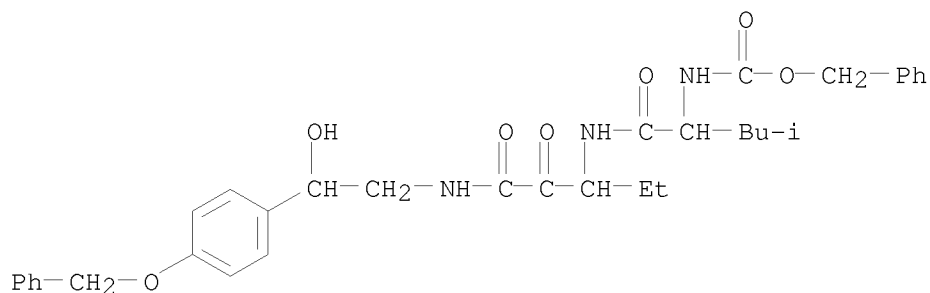
RN 153370-49-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



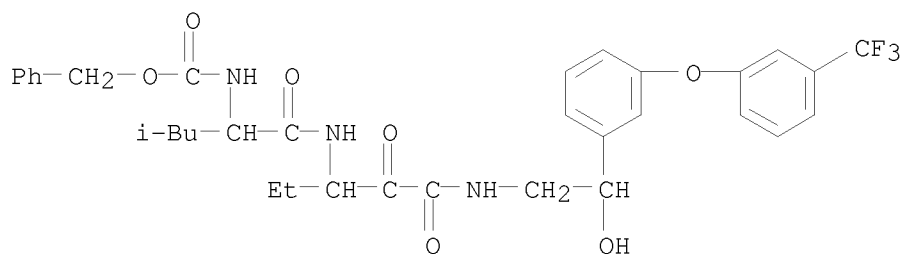
RN 153370-50-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



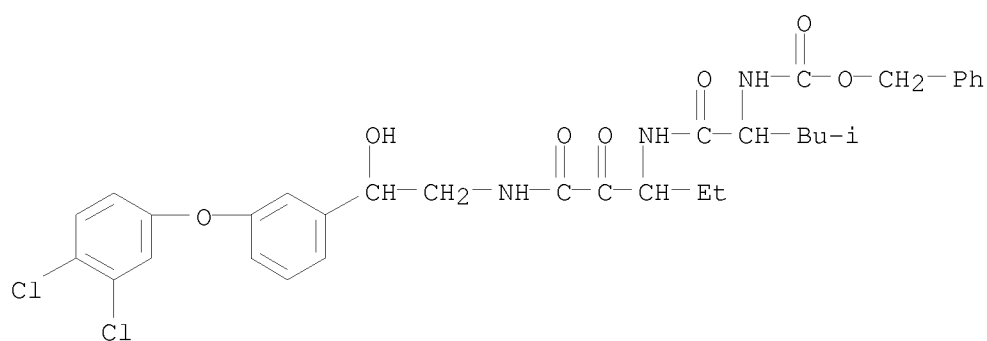
RN 153370-51-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



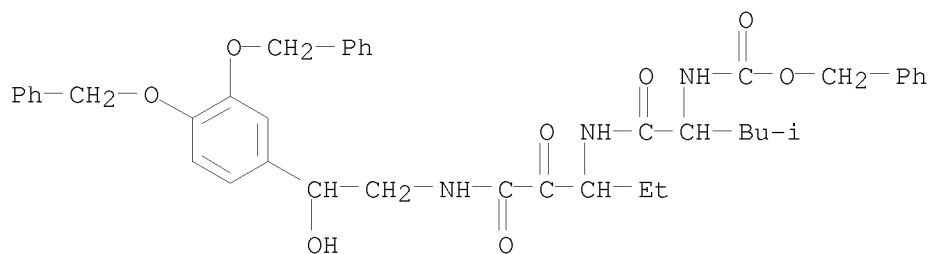
RN 153370-52-6 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



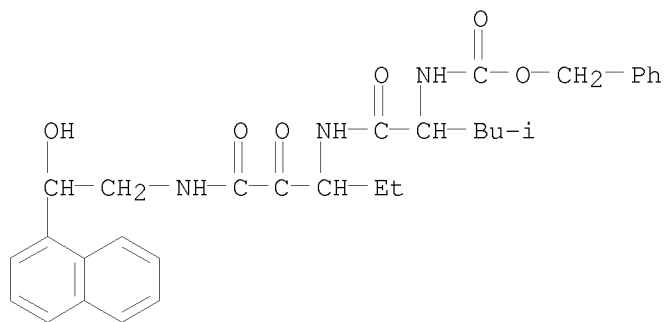
RN 153370-53-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



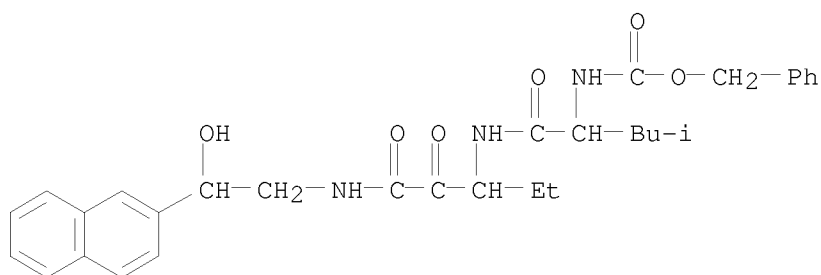
RN 153370-54-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(1-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



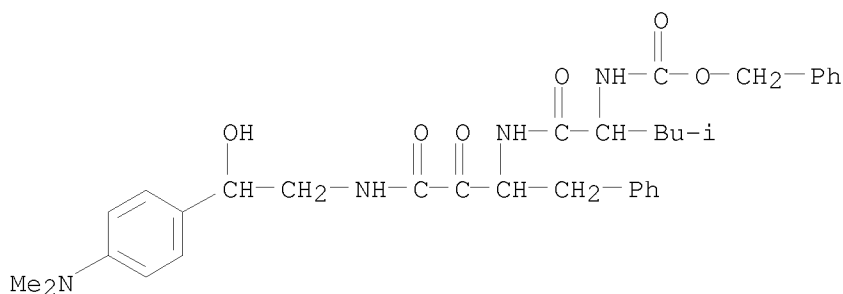
RN 153370-55-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(2-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



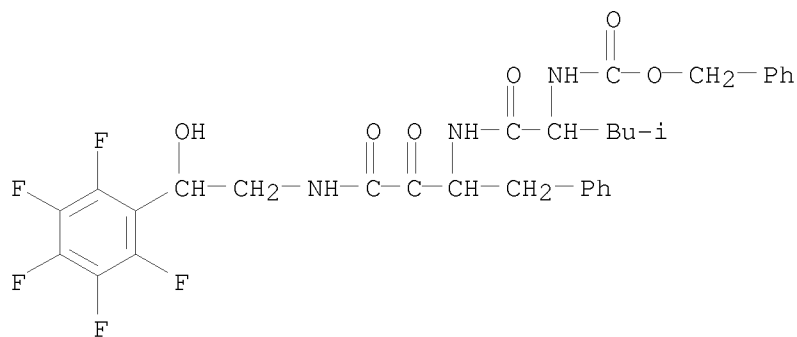
RN 153370-56-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



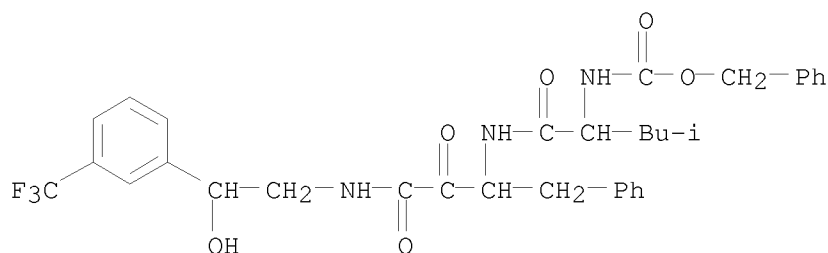
RN 153370-57-1 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



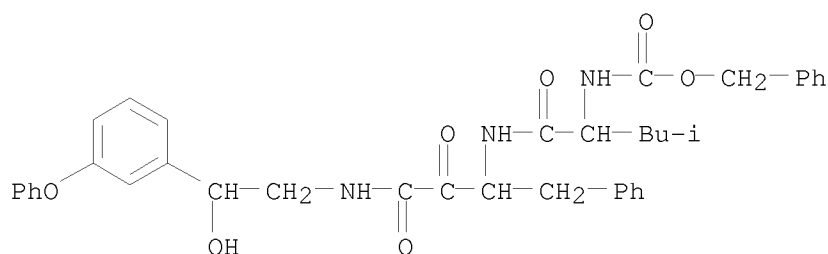
RN 153370-58-2 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-59-3 CAPLUS

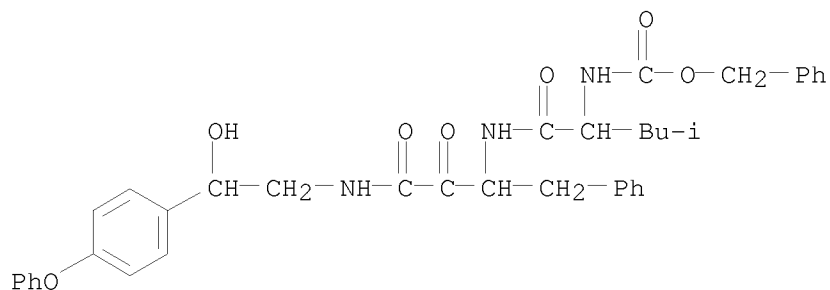
CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-60-6 CAPLUS

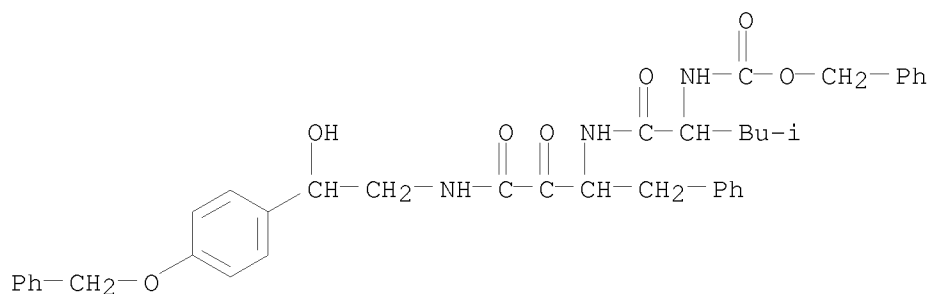
CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)





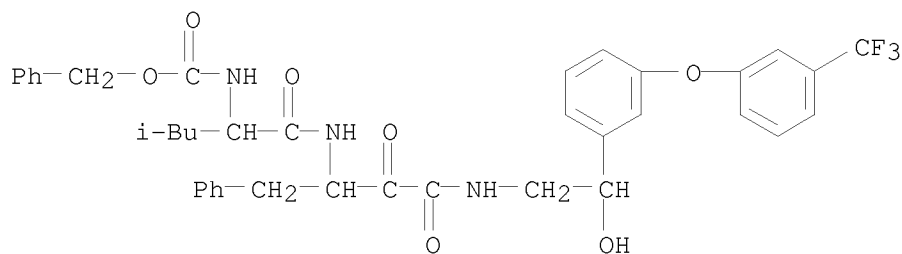
RN 153370-61-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



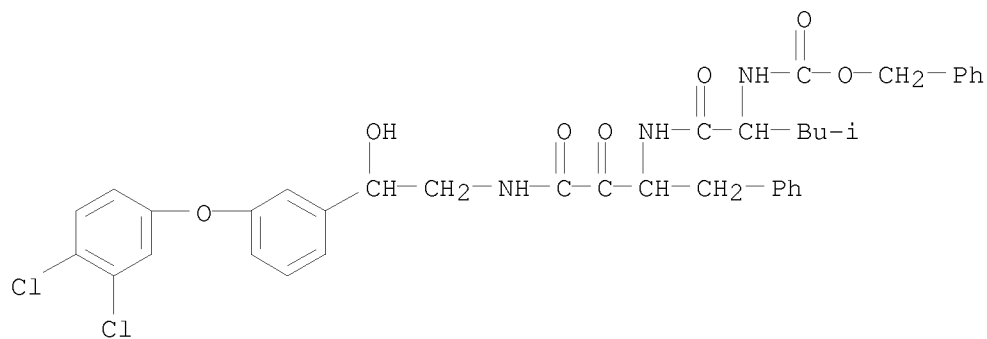
RN 153370-62-8 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



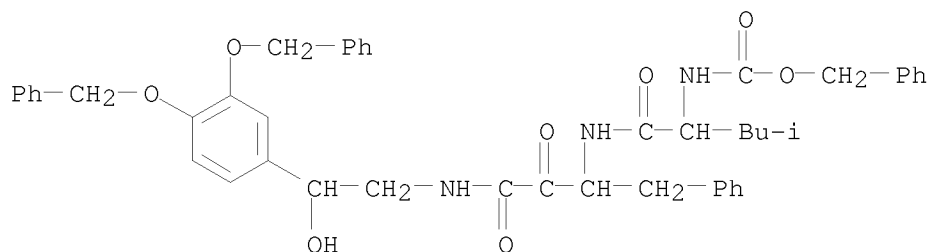
RN 153370-63-9 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



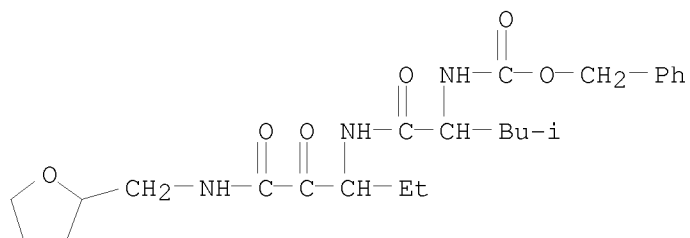
RN 153370-64-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-66-2 CAPLUS

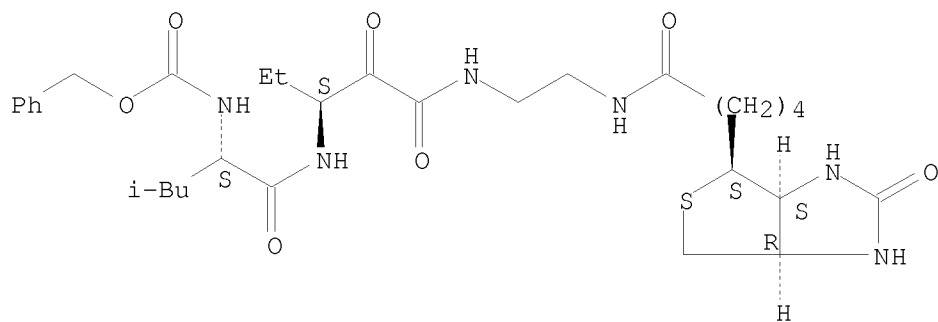
CN Carbamic acid, [1-[[[1-ethyl-3-[[tetrahydro-2-furanyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-80-0 CAPLUS

CN 2,5,9,12-Tetraazaheptadecanoic acid, 6-ethyl-17-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-3-(2-methylpropyl)-4,7,8,13-tetraoxo-, phenylmethyl ester, [3aS-[3aα,4β(3R\*,6R\*),6α]]- (9CI) (CA INDEX NAME)

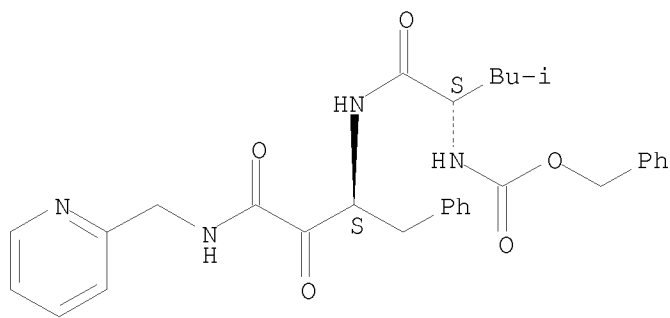
Absolute stereochemistry.



RN 153370-83-3 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

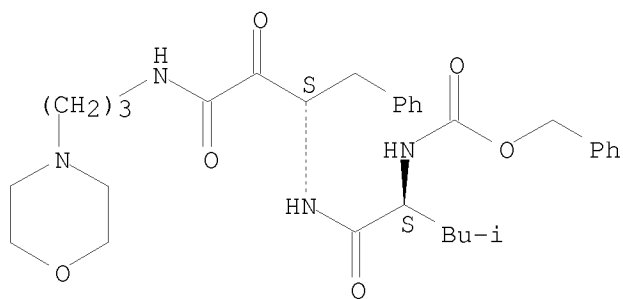
Absolute stereochemistry.



RN 153370-84-4 CAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

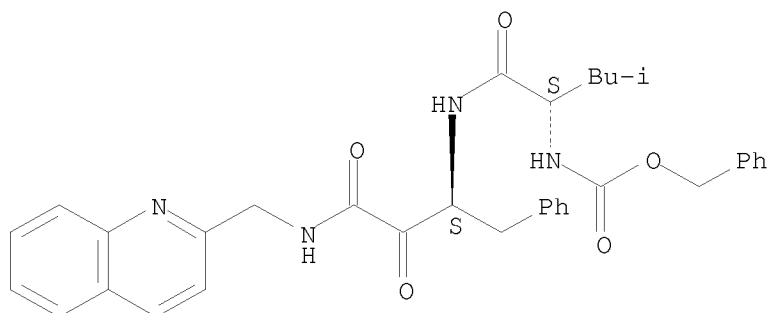
Absolute stereochemistry.



RN 153370-85-5 CAPLUS

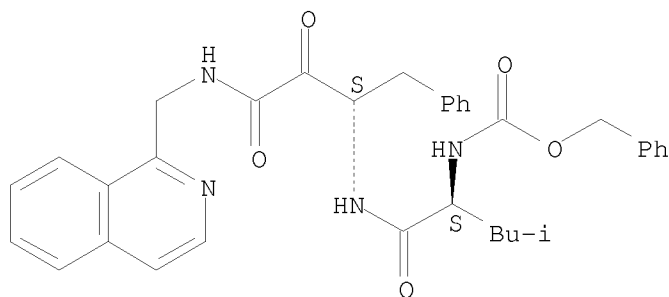
CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



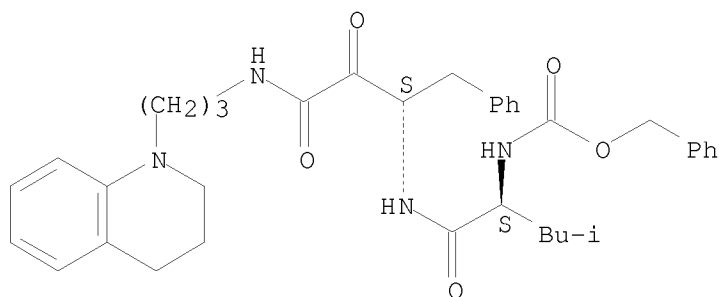
RN 153370-86-6 CAPLUS  
 CN Carbamic acid, [1-[[[3-[(1-isoquinolinylmethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



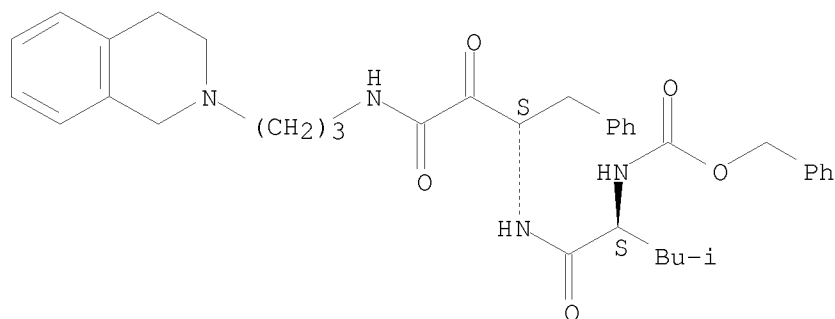
RN 153370-87-7 CAPLUS  
 CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

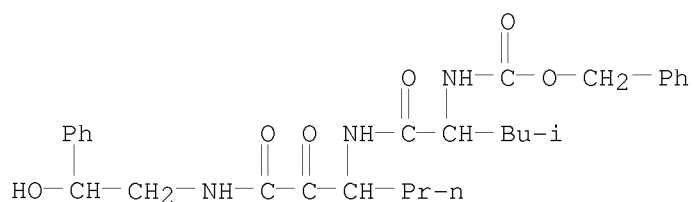


RN 153370-88-8 CAPLUS  
 CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

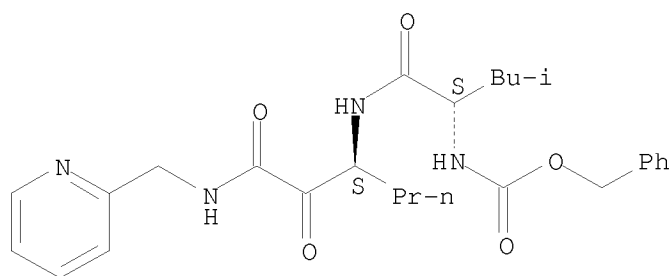


RN 153370-89-9 CAPLUS  
 CN Carbamic acid, [1-[[[1-[[[2-hydroxy-2-phenylethyl)amino]oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



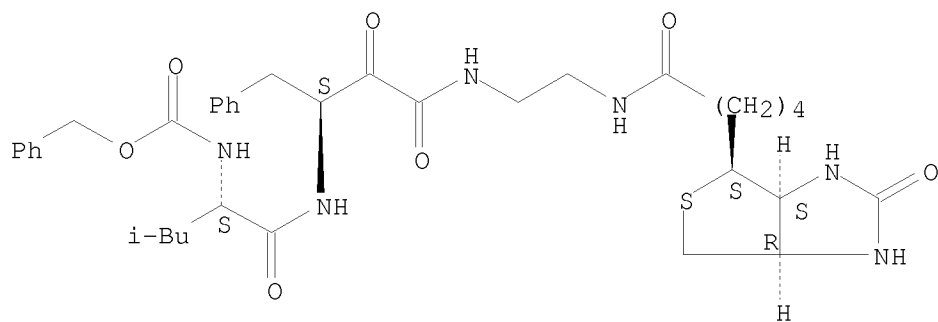
RN 153370-90-2 CAPLUS  
 CN Carbamic acid, [3-methyl-1-[[[1-[oxo[(2-pyridinylmethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-91-3 CAPLUS  
 CN 2,5,9,12-Tetraazaheptadecanoic acid, 17-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-3-(2-methylpropyl)-4,7,8,13-tetraoxo-6-(phenylmethyl)-, phenylmethyl ester, [3aS-[3aα,4β(3R\*,6R\*),6α]]- (9CI) (CA INDEX NAME)

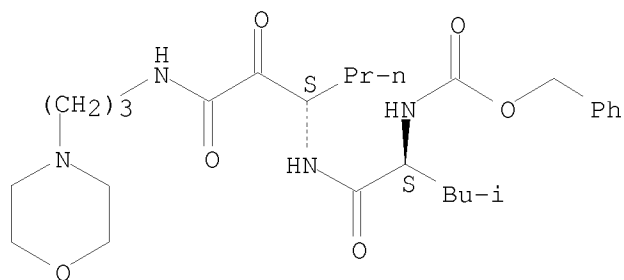
Absolute stereochemistry.



RN 153370-92-4 CAPLUS

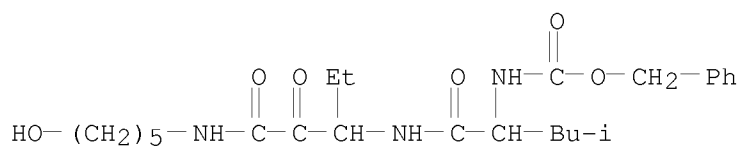
CN Carbamic acid, [3-methyl-1-[[[1-[[[3-(4-morpholinyl)propyl]amino]oxoacetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



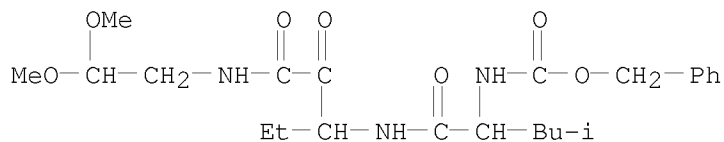
RN 178675-31-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(5-hydroxypentyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 178675-32-6 CAPLUS

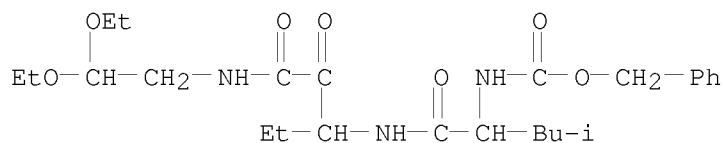
CN 12-Oxa-2,5,9-triazatridecanoic acid, 6-ethyl-11-methoxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester (CA INDEX NAME)



RN 178675-33-7 CAPLUS

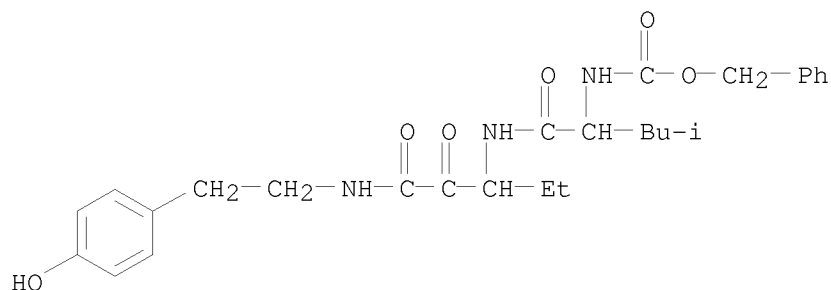
CN 12-Oxa-2,5,9-triazatetradecanoic acid, 11-ethoxy-6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester

(CA INDEX NAME)



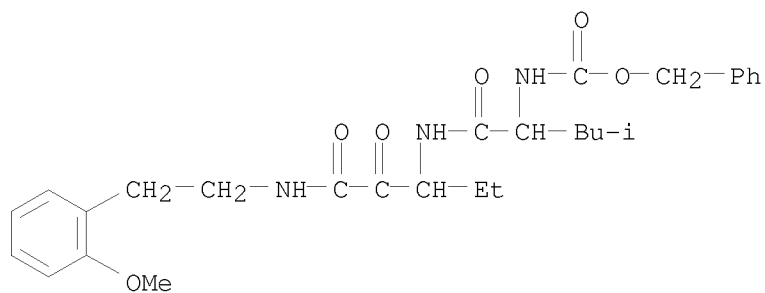
RN 178675-34-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-hydroxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



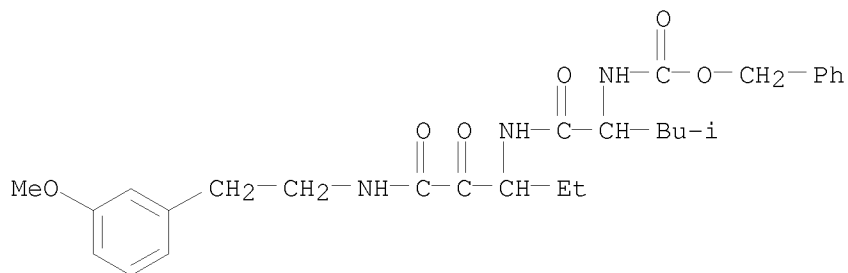
RN 178675-35-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(2-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



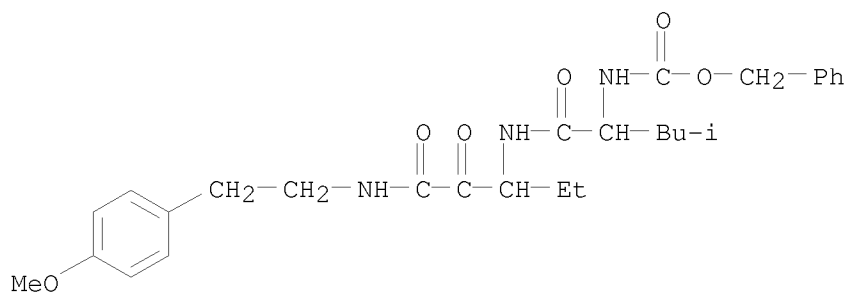
RN 178675-36-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(3-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



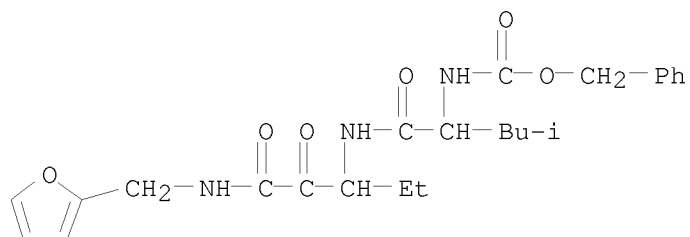
RN 178675-37-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



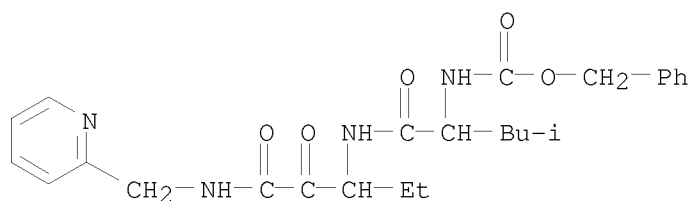
RN 178675-38-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(2-furanylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 178675-39-3 CAPLUS

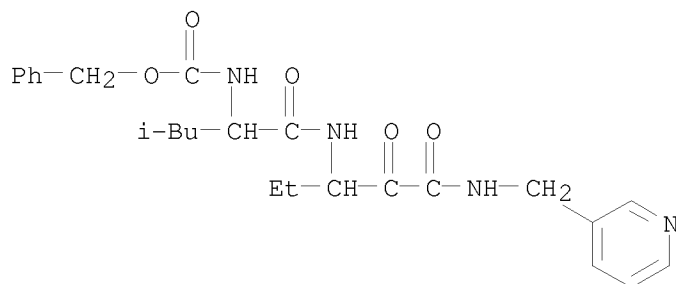
CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)





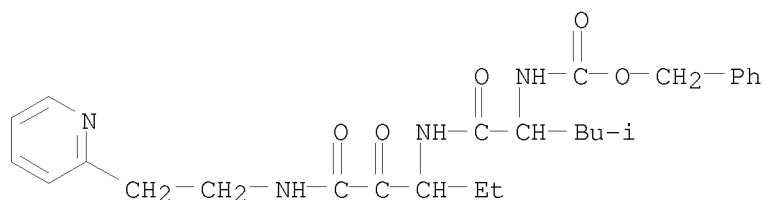
RN 178675-40-6 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(3-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



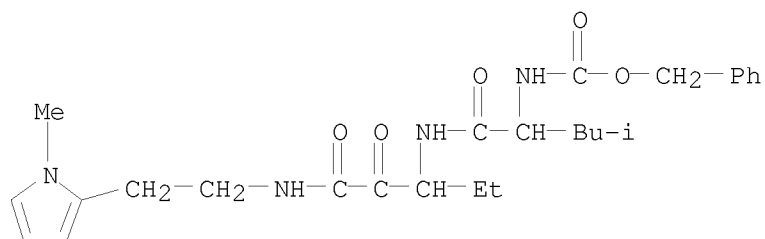
RN 178675-41-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2-(2-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



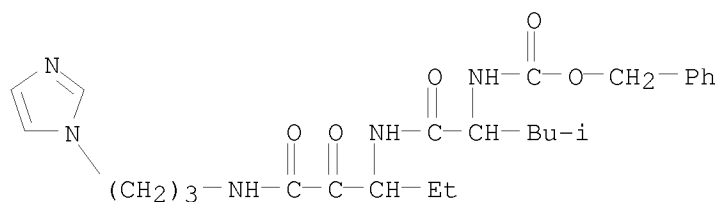
RN 178675-42-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(1-methyl-1H-pyrrol-2-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



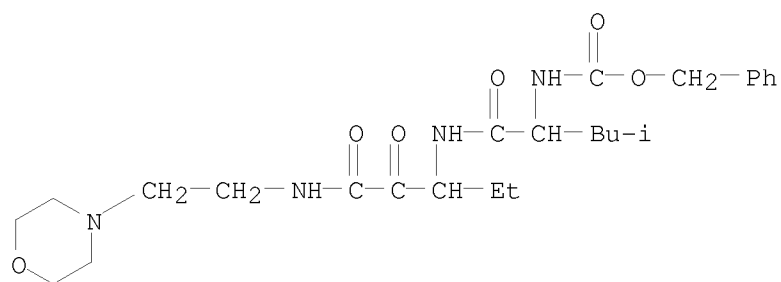
RN 178675-43-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[3-(1H-imidazol-1-yl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



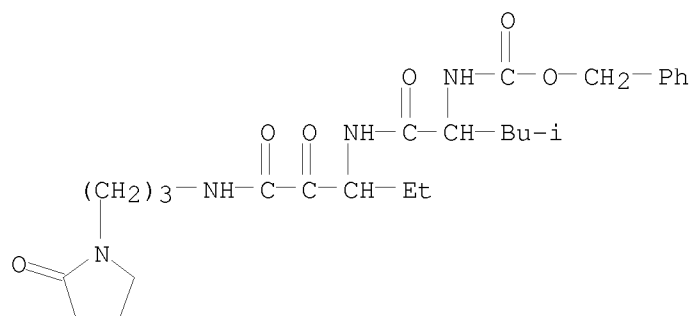
RN 178675-44-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-morpholinyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



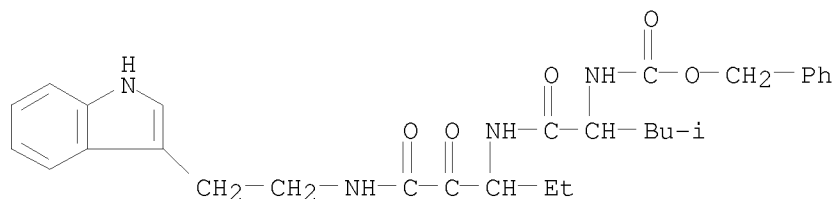
RN 178675-45-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



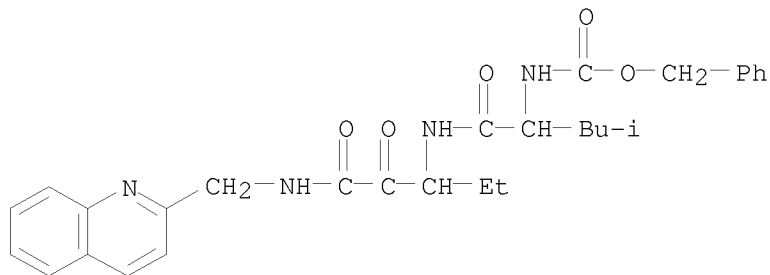
RN 178675-46-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(1H-indol-3-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



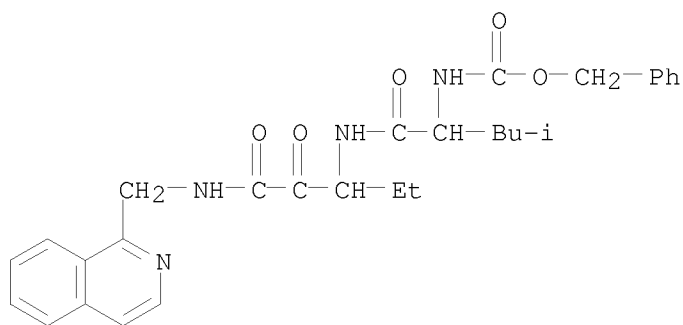
RN 178675-47-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



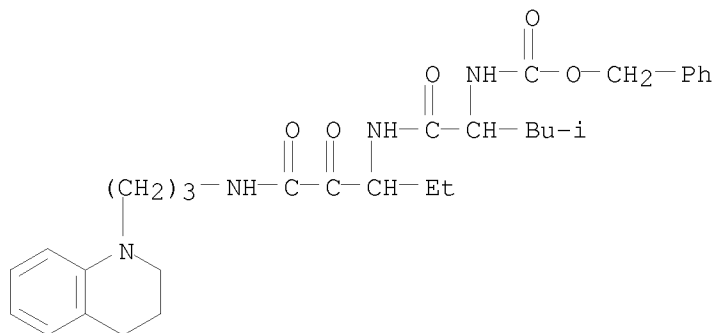
RN 178675-48-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(1-isoquinolinylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



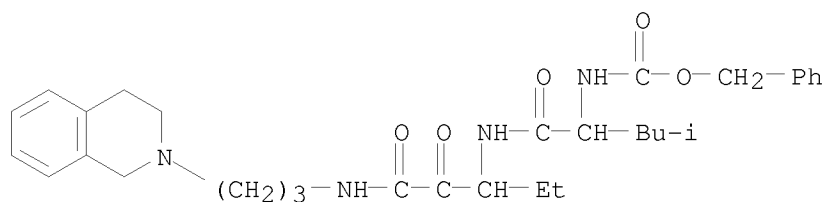
RN 178675-49-5 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



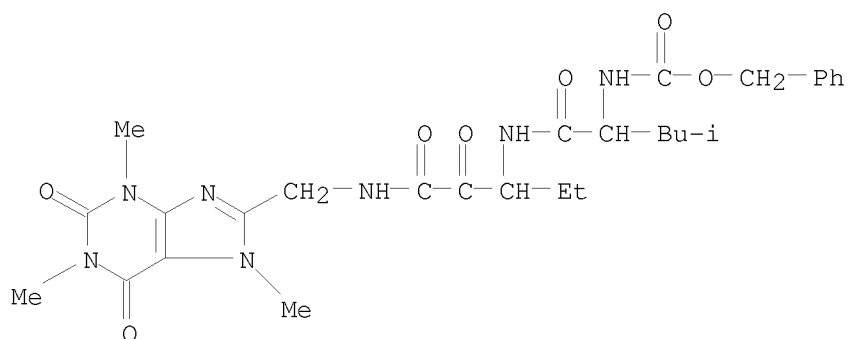
RN 178675-50-8 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



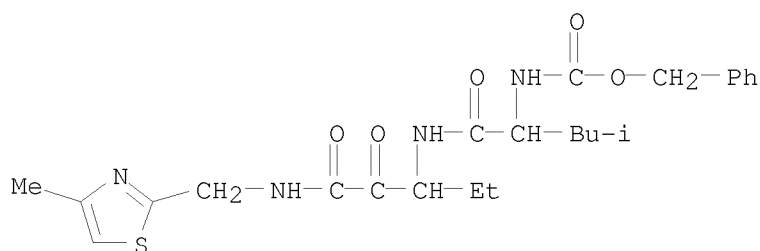
RN 178675-51-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



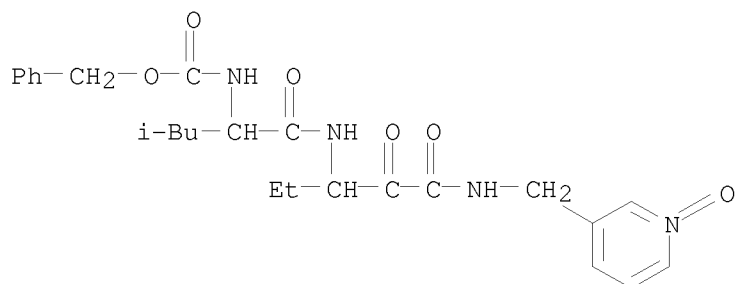
RN 178675-52-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[4-methyl-2-thiazolyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



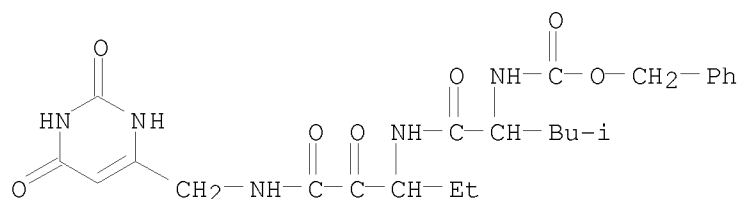
RN 178675-53-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[1-oxido-3-pyridinyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



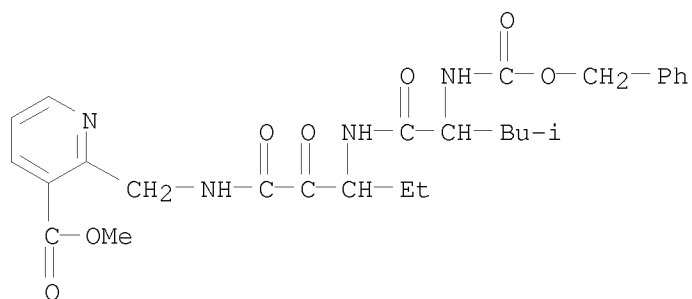
RN 178675-54-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



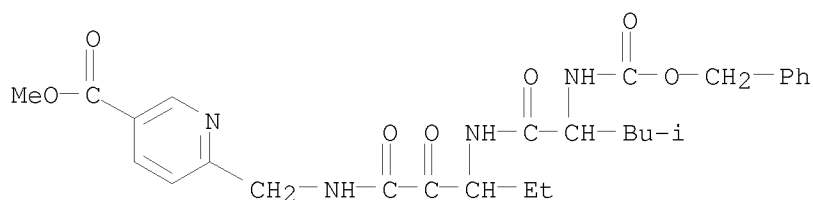
RN 178675-67-7 CAPLUS

CN 3-Pyridinecarboxylic acid, 2-[5-ethyl-8-(2-methylpropyl)-3,4,7,10-tetraoxo-12-phenyl-11-oxa-2,6,9-triazadodec-1-yl]-, methyl ester (CA INDEX NAME)



RN 178675-68-8 CAPLUS

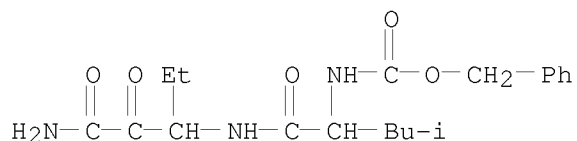
CN 3-Pyridinecarboxylic acid, 6-[5-ethyl-8-(2-methylpropyl)-3,4,7,10-tetraoxo-12-phenyl-11-oxa-2,6,9-triazadodec-1-yl]-, methyl ester (CA INDEX NAME)



RN 178675-69-9 CAPLUS

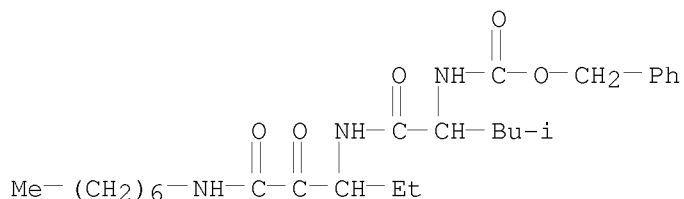
CN Carbamic acid, [1-[[3-amino-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-

methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



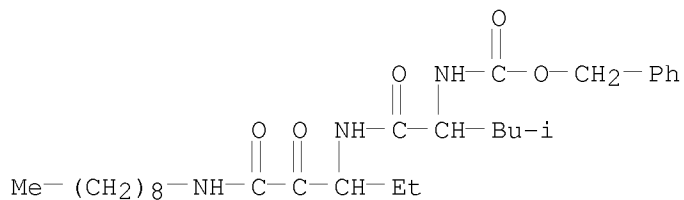
RN 178675-70-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(heptylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



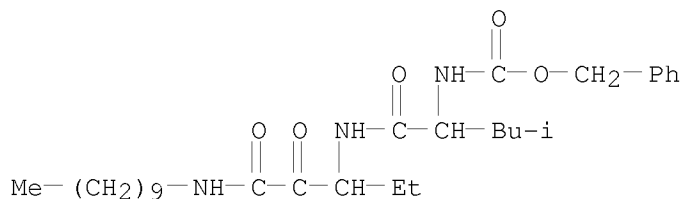
RN 178675-71-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(nonylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



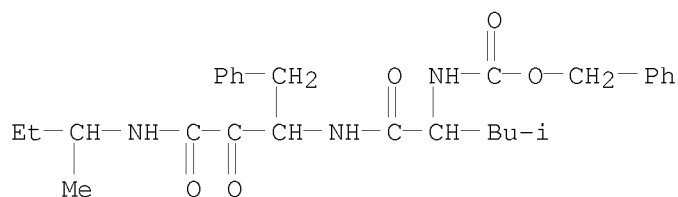
RN 178675-72-4 CAPLUS

CN Carbamic acid, [1-[[[3-(decylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 178675-73-5 CAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-[(1-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



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ACCESSION NUMBER: 1996:241147 CAPLUS

DOCUMENT NUMBER: 124:307407

ORIGINAL REFERENCE NO.: 124:56695a,56698a

TITLE: Calpain inhibitor AK295 attenuates motor and cognitive deficits following experimental brain injury in the rat

AUTHOR(S): Saatman, Kathryn E.; Murai, Hisayuki; Bartus, Raymond T.; Smith, Douglas H.; Hayward, Neil J.; Perri, Brian; McIntosh, Tracy K.

CORPORATE SOURCE: Div. Neurosurgery, Univ. Pennsylvania, Philadelphia, PA, 19104, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(8), 3428-33

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Marked increases in intracellular calcium may play a role in mediating cellular dysfunction and death following central nervous system trauma, in part through the activation of the calcium-dependent neutral protease calpain. In this study, we evaluated the effect of the calpain inhibitor AK295 [Z-Leu-aminobutyric acid-CONH(CH<sub>2</sub>)<sub>3</sub>-morpholine] on cognitive and motor deficits following lateral fluid percussion brain injury in rats. Before injury, male Sprague-Dawley rats (350-425 g) were trained to perform a beam-walking task and to learn a cognitive test using a Morris water maze paradigm. Animals were subjected to fluid percussion injury (2.2-2.4 atm; 1 atm = 101.3 kPa) and, beginning at 15 min postinjury, received a continuous intraarterial infusion of AK295 (120-140 mg/kg) or vehicle for 48 h. Sham (uninjured) animals received either drug or vehicle. Animals were evaluated for neurobehavioral motor function at 48 h and 7 days post-injury and were tested in the Morris water maze to evaluate memory retention at 7 days post-injury. At 48 h, both vehicle- and AK295-treated injured animals showed significant motor dysfunction. However, brain-injured, AK295-treated animals showed markedly improved motor scores, which were not significantly different from sham (uninjured) animals. Vehicle-treated, injured animals demonstrated a profound cognitive deficit, which was significantly attenuated by AK295 treatment. To our knowledge, this study is the first to use a calpain inhibitor following brain trauma and suggests that calpain plays a role in the posttraumatic events underlying memory and neuromotor dysfunction.

IT 160399-35-9, AK 295

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

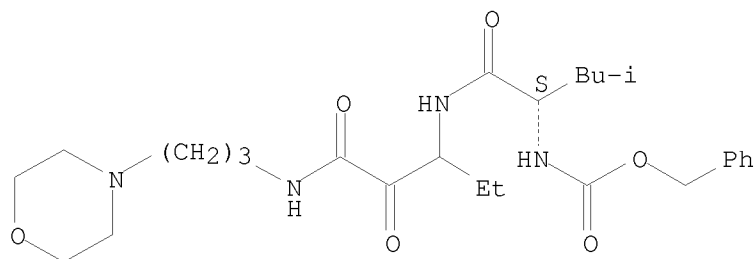
(calpain inhibitor AK295 attenuates motor and cognitive deficits following exptl. brain injury in rat)

RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA

INDEX NAME)

Absolute stereochemistry.  
Currently available stereo shown.



L10 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:731521 CAPLUS

DOCUMENT NUMBER: 123:144653

ORIGINAL REFERENCE NO.: 123:25801a, 25804a

TITLE: Preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors.

INVENTOR(S): Harbeson, Scott L.; Straub, Julie Ann

PATENT ASSIGNEE(S): Alkermes, Inc., USA

SOURCE: PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500535	A1	19950105	WO 1994-US6497	19940609 <--
W:	AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5541290	A	19960730	US 1993-82274	19930624 <--
AU 9472452	A	19950117	AU 1994-72452	19940609 <--
PRIORITY APPLN. INFO.:			US 1993-82274	A 19930624 <--
			WO 1994-US6497	W 19940609 <--

OTHER SOURCE(S): CASREACT 123:144653; MARPAT 123:144653

AB M(A1)xA2NHCHR1COCONHR2SO2R3 (sic), M(A1)xA2NHCHR1COCONHR5R6, etc.; [M = H, H2NCO, H2NCS, H2NSO2, R7CS, R7NHCS, R7CO, R7SO2, R7O2C, etc.; R7 = 1-adamantyl, (substituted) alkyl, alkyl, Ph, naphthyl, phenylalkyl, phenoxyalkyl, etc.; A1 = D-, L-, or nonchiral amino acid, e.g., Ala, Val, Leu, Ile, Met, Tyr, Asn, Gln,  $\beta$ -Ala, Sar, Orn, O-ethylserine, pipecolic acid, cyclohexylalanine, pyridylalanine, p-nitrophenylalanine,  $\alpha$ -aminoheptanoic acid, citrulline, 2-azetidinecarboxylic acid, trifluoroleucine, etc.; x = 0-3; A2 = D- or L-amino acid capable of imparting calpain specificity; R1 = alkyl, cycloalkyl, fluoroalkyl; R2 = alkyl, cycloalkyl, phenylalkyl, (substituted) phenylalkyl, phenylcycloalkyl; R3 = R2, OH, OR2, NH2, NHR2; NR2R2; R5, R6 = H, alkyl, cycloalkyl, (substituted) phenylalkyl, phenylcycloalkyl, morpholinoalkyl, piperidinoalkyl, etc.], were prepared Thus, Z-Leu-Abu-CONHET (Abu = L- $\alpha$ -aminobutyric acid) (solution phase preparation given) inhibited calpain I with Ki = 77 nM.

IT 144231-76-5P 144248-93-1P 153371-08-5P  
160801-90-1P 160801-91-2P 160801-92-3P



161021-87-0P 166195-97-7P 166195-98-8P

166195-99-9P 166196-00-5P

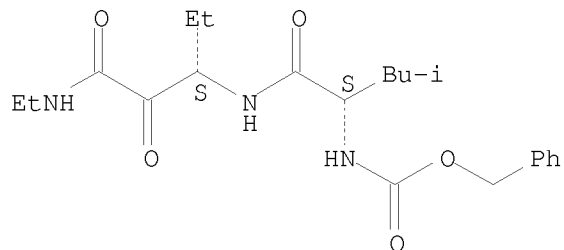
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors)

RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

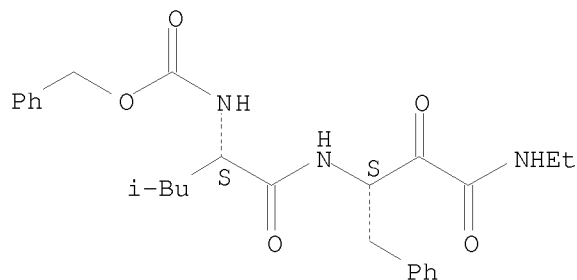
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

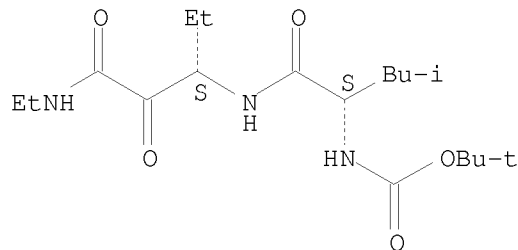
Absolute stereochemistry.



RN 153371-08-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

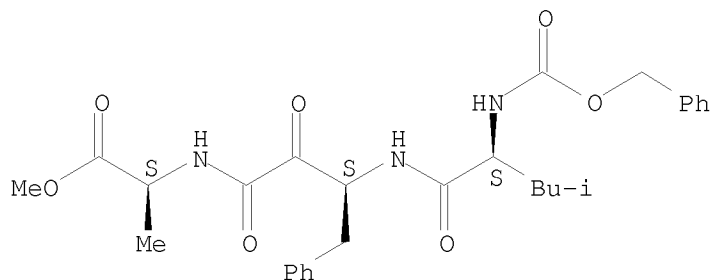
Absolute stereochemistry.



RN 160801-90-1 CAPLUS

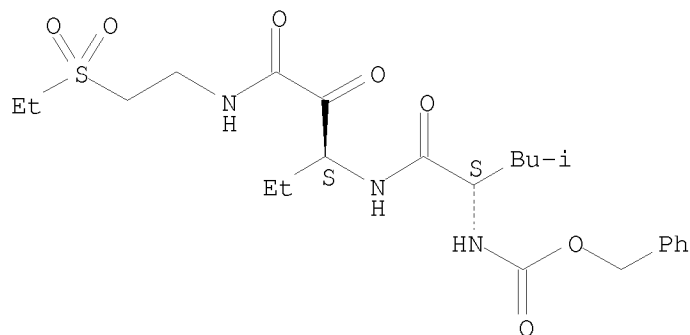
CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-  
[[ (phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-,  
methyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



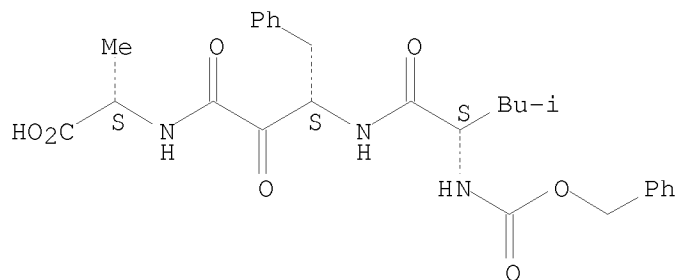
RN 160801-91-2 CAPLUS  
CN 12-Thia-2,5,9-triazatetradecanoic acid,  
6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester,  
12,12-dioxide, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



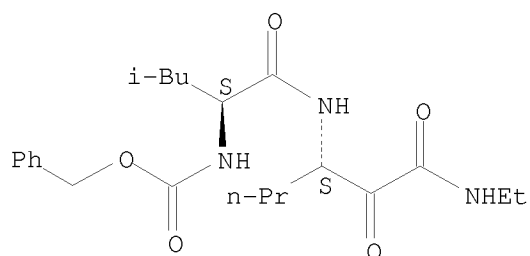
RN 160801-92-3 CAPLUS  
CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-  
[[ (phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-,  
[S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



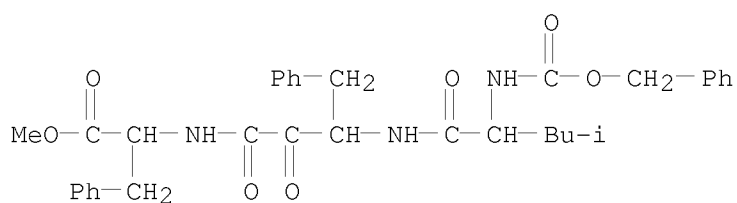
RN 161021-87-0 CAPLUS  
CN Carbamic acid, [1-[[[1-[(ethylamino)oxoacetyl]butyl]amino]carbonyl]-3-  
methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



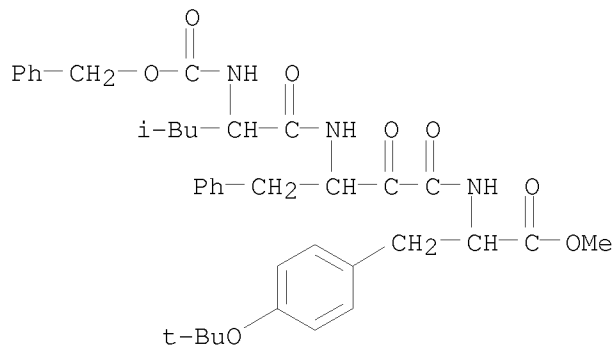
RN 166195-97-7 CAPLUS

CN L-Phenylalanine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-, methyl ester (9CI) (CA INDEX NAME)



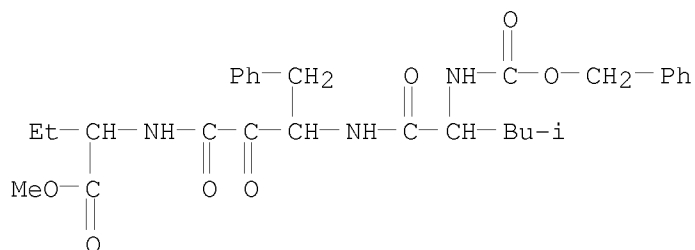
RN 166195-98-8 CAPLUS

CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-O-(1,1-dimethylethyl)-, methyl ester (9CI) (CA INDEX NAME)

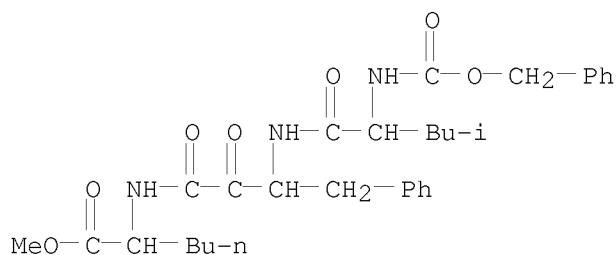


RN 166195-99-9 CAPLUS

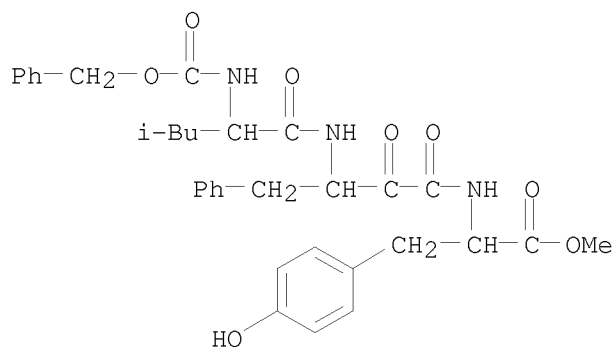
CN Butanoic acid, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-L-2-amino-, methyl ester (9CI) (CA INDEX NAME)



RN 166196-00-5 CAPLUS  
 CN L-Norleucine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-, methyl ester (9CI) (CA INDEX NAME)



IT 848487-37-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors)  
 RN 848487-37-6 CAPLUS  
 CN 2-Oxa-4,7,11-triazatridecan-13-oic acid,  
 12-[(4-hydroxyphenyl)methyl]-5-(2-methylpropyl)-3,6,9,10-tetraoxo-1-phenyl-  
 8-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1995:223078 CAPLUS  
 DOCUMENT NUMBER: 122:23465  
 ORIGINAL REFERENCE NO.: 122:4457a,4460a  
 TITLE: Calpain inhibitor AK295 protects neurons from focal  
 brain ischemia: effects of postocclusion  
 intra-arterial administration  
 AUTHOR(S): Bartus, Raymond T.; Hayward, Neil J.; Elliott, Peter  
 J.; Sawyer, Sean D.; Baker, Keith L.; Dean, Reginald  
 L.; Akiyama, Alan; Straub, Julie A.; Harbeson, Scott  
 L.; et al.  
 CORPORATE SOURCE: Received February, Cambridge, MA, 02139, USA  
 SOURCE: Stroke (1994), 25(11), 2265-70  
 CODEN: SJCCA7; ISSN: 0039-2499  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB This research was performed to determine whether a selective inhibitor of the  
 calcium-dependent protease, calpain, could reduce ischemia-associated brain  
 damage when peripherally administered after a vascular occlusion. A  
 variation of the rat middle cerebral artery occlusion model was used. A  
 range of doses of AK295 (a novel calpain inhibitor synthesized for this  
 purpose) was continuously infused through the internal carotid artery,

beginning 1.25 h from the initiation of the occlusion. Rats were killed at 21 h, and the infarct volume was quantified. Postocclusion (1.25-h) infusion of the calpain inhibitor AK295 elicited a dose-dependent neuroprotective effect after focal ischemia. The highest dose tested (3 mg/kg per h) afforded the maximum effect, illustrated by a 32% reduction in infarct volume 21 h after the ischemia (vehicle, 81.7±4.7 mm<sup>3</sup>; AK295, 54.9±6.9 mm<sup>3</sup>; P<.007). These data provide the first evidence that a peripherally administered calpain inhibitor can protect against ischemic brain damage. They offer further support for an important role of calpain proteolysis in the brain degeneration associated with cerebral ischemic events and suggest that selective calpain inhibitors provide a rational, novel, and viable means of treating such neurodegenerative problems.

IT 160399-35-9, AK 295

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

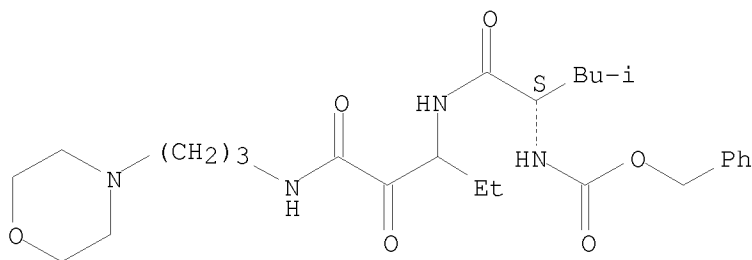
(calpain inhibitor AK295 protects neurons from focal brain ischemia)

RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Currently available stereo shown.



L10 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:194154 CAPLUS

DOCUMENT NUMBER: 122:89584

ORIGINAL REFERENCE NO.: 122:16795a,16798a

TITLE: High-performance liquid chromatographic reversed-phase and normal-phase separation of diastereomeric  $\alpha$ -ketoamide calpain inhibitors

AUTHOR(S): Wu, Chichih; Akiyama, Alan; Straub, Julie Ann

CORPORATE SOURCE: Alkermes, Inc., Cambridge, MA, 02139, USA

SOURCE: Journal of Chromatography, A (1994), 684(2), 243-9

CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

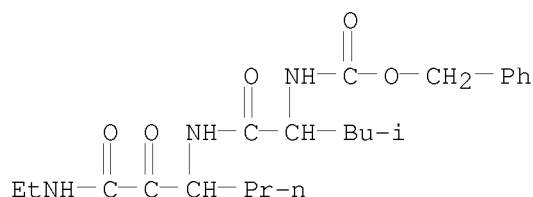
AB  $\alpha$ -Ketoamide calpain inhibitors contain a stereochem. labile chiral center adjacent to the keto moiety, which when epimerized results in diastereomers. High-temperature C4 reversed-phase HPLC methods were developed for anal. of general purity of  $\alpha$ -ketoamide calpain inhibitors and resulted in the separation of diastereomers of the pos. charged inhibitor, AK295. Normal-phase methods that employed a Nucleosil Chiral-2 column were developed for separation of diastereomers of uncharged  $\alpha$ -ketoamides. These methods used conditions in which the keto moiety of the inhibitors was minimally affected by the mobile phase.

IT 160299-89-8, AK 311 160399-35-9, AK 295

RL: ANT (Analyte); ANST (Analytical study)  
(HPLC for separation of diastereomeric  $\alpha$ -keto amide calpain inhibitors)

RN 160299-89-8 CAPLUS

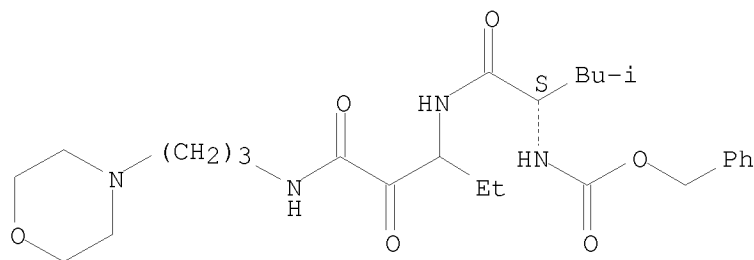
CN Carbamic acid, [1-[[[1-[(ethylamino)oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 160399-35-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Currently available stereo shown.



L10 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:31017 CAPLUS

DOCUMENT NUMBER: 122:133766

ORIGINAL REFERENCE NO.: 122:24963a,24966a

TITLE: Stereospecific Synthesis of Peptidyl  $\alpha$ -Keto Amides as Inhibitors of Calpain

AUTHOR(S): Harbeson, Scott L.; Abelleira, Susan M.; Akiyama, Alan; Barrett, Robert, III; Carroll, Renee M.; Straub, Julie Ann; Tkacz, Jaroslaw N.; Wu, Chichih; Musso, Gary F.

CORPORATE SOURCE: Alkermes Inc., Cambridge, MD, 02139-4136, USA

SOURCE: Journal of Medicinal Chemistry (1994), 37(18), 2918-29

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peptidyl  $\alpha$ -keto amides have been synthesized and tested as inhibitors of the cysteine protease calpain. A stereospecific synthesis was devised in which protected dipeptidyl  $\alpha$ -hydroxy amides were oxidized with TEMPO/hypochlorite to the corresponding  $\alpha$ -keto amides. This oxidation was accomplished in good yields and without epimerization of the chiral center adjacent to the ketone. The potent inhibition of porcine calpain I by the L,L diastereomers, combined with the poor inhibition by the L,D diastereomers, established the requirement for the all-L stereochem. of the active inhibitor. The early lead inhibitors were

very hydrophobic and, therefore, poorly soluble in aqueous solns. Using the stereospecific route, new compds. were prepared with polar groups at the C- and N-termini. These modifications resulted in more soluble inhibitors that were still potent inhibitors of calpain. Studies of the stability of these  $\alpha$ -keto amides showed that absolute stereochem. can be maintained in acidic and unbuffered environments but general base-catalyzed epimerization of the chiral center adjacent to the ketone occurred rapidly. The  $\alpha$ -hydroxy precursors were inactive as inhibitors of calpain, which supports the hypothesis that the  $\alpha$ -keto compds. reversibly form an enzyme-bound tetrahedral species that results from the nucleophilic addition of the catalytic thiol of calpain to the electrophilic ketone of the inhibitor.

IT 144231-76-5P 144248-93-1P 153371-08-5P  
160801-71-8P 160801-90-1P 160801-91-2P  
160801-92-3P 160868-23-5P 161021-87-0P  
161021-88-1P

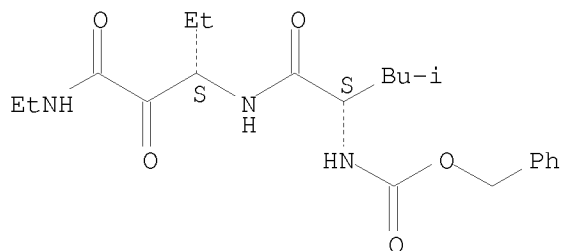
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(stereospecific synthesis of peptidyl  $\alpha$ -keto amides as inhibitors of calpain)

RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

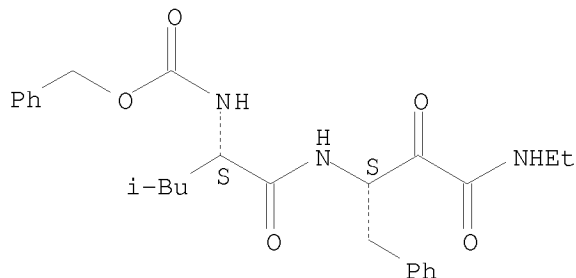
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

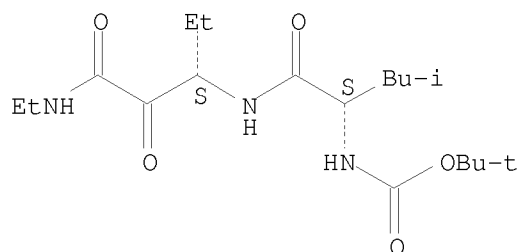
Absolute stereochemistry.



RN 153371-08-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

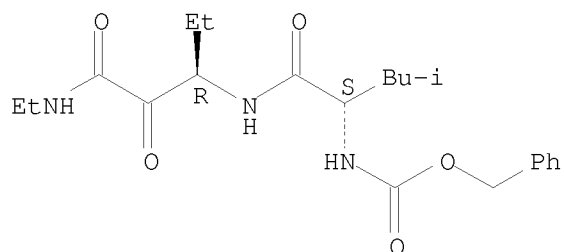
Absolute stereochemistry.



RN 160801-71-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

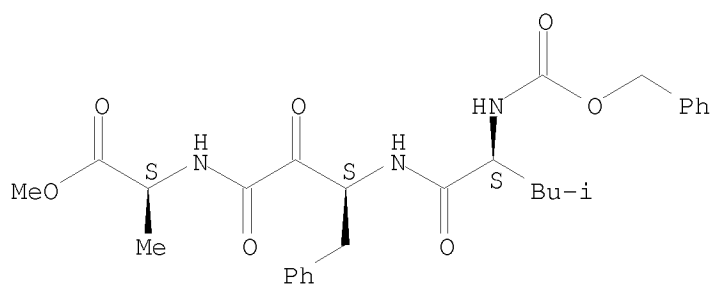
Absolute stereochemistry.



RN 160801-90-1 CAPLUS

CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-[[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-, methyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

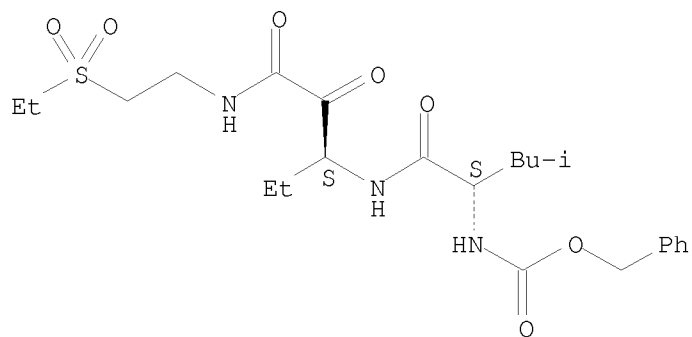


RN 160801-91-2 CAPLUS

CN 12-Thia-2,5,9-triazatetradecanoic acid, 6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, 12,12-dioxide, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

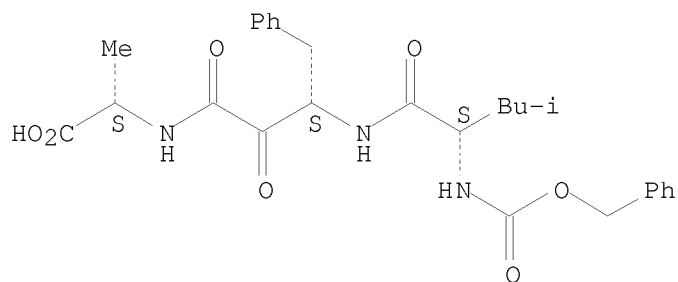
Absolute stereochemistry.





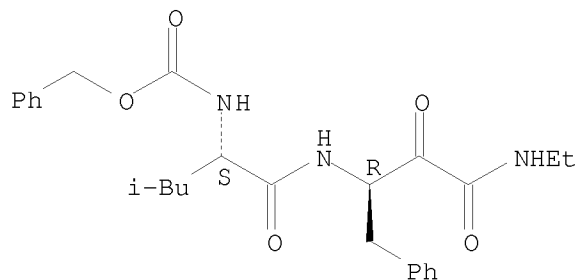
RN 160801-92-3 CAPLUS  
 CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-  
 [[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-,  
 [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



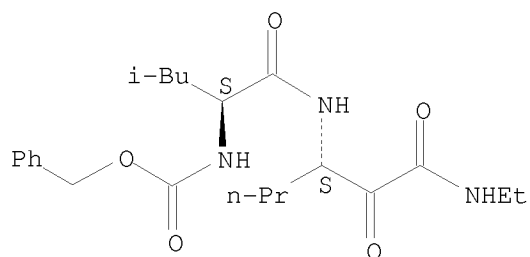
RN 160868-23-5 CAPLUS  
 CN Carbamic acid, [1-[[[3-(ethylamino)-2,3-dioxo-1-  
 (phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester,  
 [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



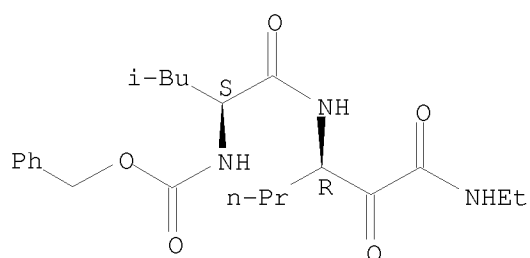
RN 161021-87-0 CAPLUS  
 CN Carbamic acid, [1-[[[1-[(ethylamino)oxoacetyl]butyl]amino]carbonyl]-3-  
 methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 161021-88-1 CAPLUS  
 CN Carbamic acid, [1-[[[1-[(ethylamino)oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1994:153723 CAPLUS  
 DOCUMENT NUMBER: 120:153723  
 ORIGINAL REFERENCE NO.: 120:26825a,26828a  
 TITLE: Use of calpain inhibitors in the inhibition and treatment of medical conditions associated with increased calpain activity  
 INVENTOR(S): Eveleth, David D., Jr.; Lynch, Gary; Powers, James C.; Bartus, Raymond T.  
 PATENT ASSIGNEE(S): Cortex Pharmaceuticals, Inc., USA; Georgia Tech Research Corp.  
 SOURCE: PCT Int. Appl., 255 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9400095	A2	19940106	WO 1993-US6143	19930624 <--
WO 9400095	A3	19940317		
W:	AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9345449	A	19940124	AU 1993-45449	19930624 <--
JP 09500087	T	19970107	JP 1993-502621	19930624 <--
PRIORITY APPLN. INFO.:			US 1992-903800	A2 19920624 <--
			US 1993-34996	A2 19930316 <--
			US 1993-72609	A2 19930601 <--

AB Medical conditions in mammals (e.g. cardiac muscle tissue damage, cataracts, smooth muscle damage, and vasospasm) associated with increased proteolytic activity of calpain are treated by administering a pharmaceutical composition containing a calpain inhibitor in a pharmacol.

effective

amount The inhibitor is a peptide keto compound, substituted heterocyclic compound, or halo ketone peptide. Also, a method of inhibiting proliferation of smooth muscle cells and thereby preventing the restenosis of a blood vessel which has undergone therapeutic angioplasty includes the administration of a calpain inhibitor to the blood vessel during or after the angioplasty. Further, methods of blocking the establishment of the tonically contracted state in smooth muscle and relaxing tonically contracted smooth muscle are disclosed. These methods involve the administration of a calpain inhibitor, thereby reducing or preventing smooth muscle contraction associated with vasospasm and bronchospasm.

IT 144231-72-1 144231-73-2 144231-74-3  
 144231-75-4 144231-76-5 144231-77-6  
 144231-78-7 144231-79-8 144231-80-1  
 144231-81-2 144231-82-3 144231-83-4  
 144231-84-5 144231-85-6 144248-93-1  
 144248-94-2 144248-95-3 144248-96-4  
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 153370-47-9 153370-48-0 153370-49-1  
 153370-50-4 153370-51-5 153370-52-6  
 153370-53-7 153370-54-8 153370-55-9  
 153370-56-0 153370-57-1 153370-58-2  
 153370-59-3 153370-60-6 153370-61-7  
 153370-62-8 153370-63-9 153370-64-0  
 153370-65-1 153370-66-2 153370-67-3  
 153370-68-4 153370-69-5 153370-70-8  
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 153370-83-3 153370-84-4 153370-85-5  
 153370-86-6 153370-87-7 153370-88-8  
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 153370-92-4 153371-08-5

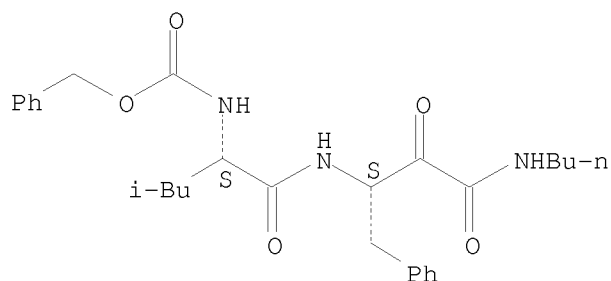
RL: BIOL (Biological study)

(as calpain inhibitor, heart and vascular disease treatment with)

RN 144231-72-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

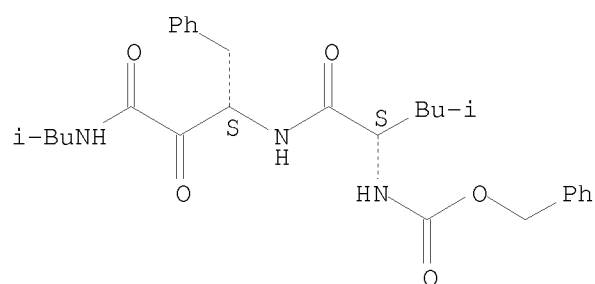
Absolute stereochemistry.



RN 144231-73-2 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-[(2-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

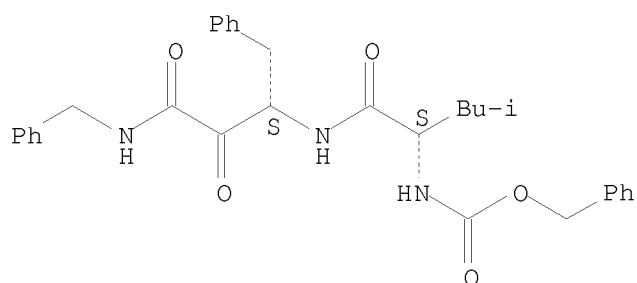
Absolute stereochemistry.



RN 144231-74-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

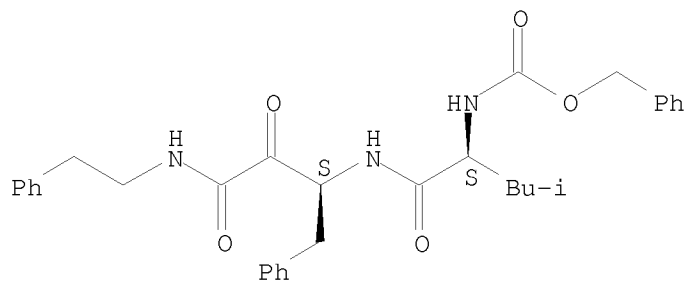
Absolute stereochemistry.



RN 144231-75-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

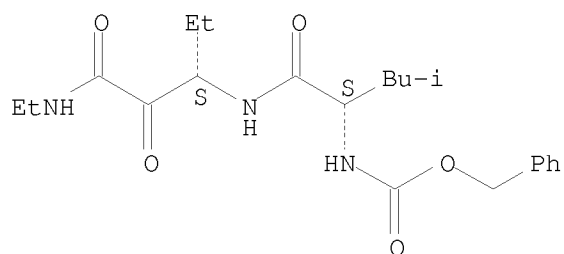
Absolute stereochemistry.



RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

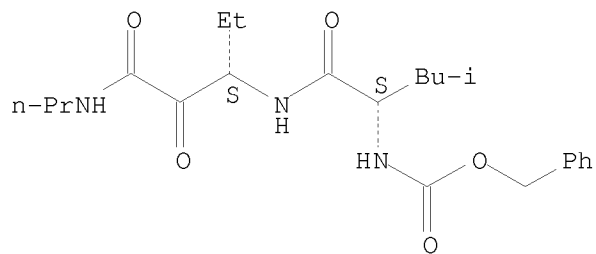
Absolute stereochemistry.



RN 144231-77-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

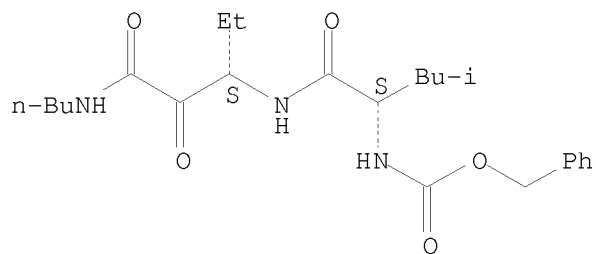
Absolute stereochemistry.



RN 144231-78-7 CAPLUS

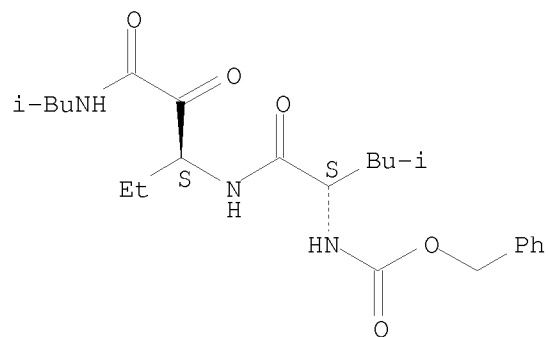
CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



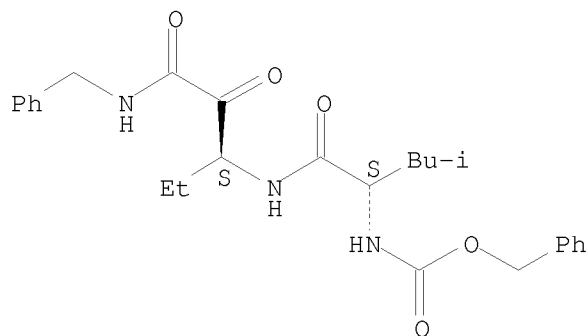
RN 144231-79-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



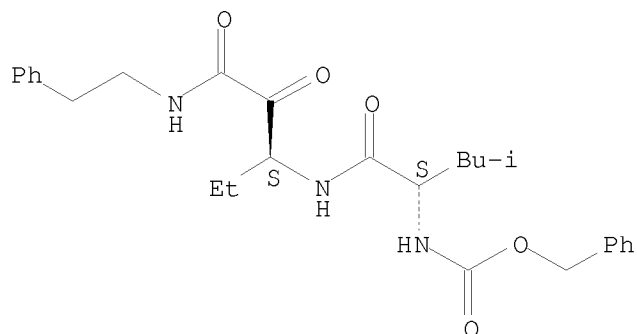
RN 144231-80-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144231-81-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

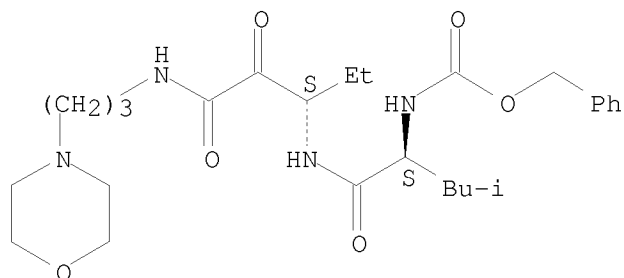
Absolute stereochemistry.



RN 144231-82-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)

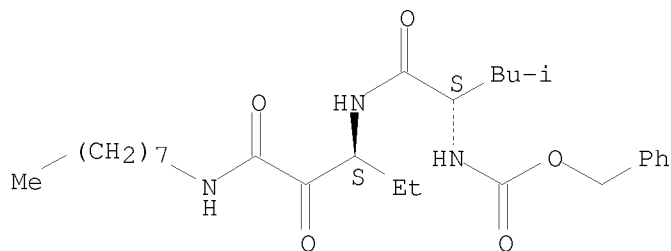
Absolute stereochemistry.



RN 144231-83-4 CAPLUS

CN	Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)
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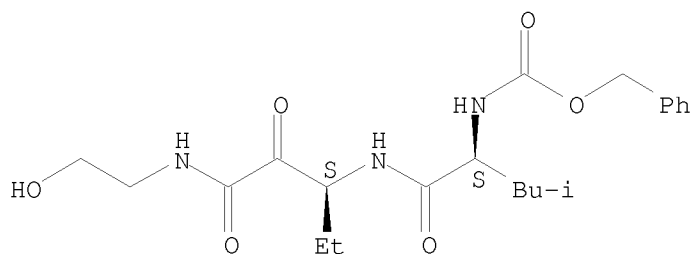
Absolute stereochemistry.



RN 144231-84-5 CAPLUS

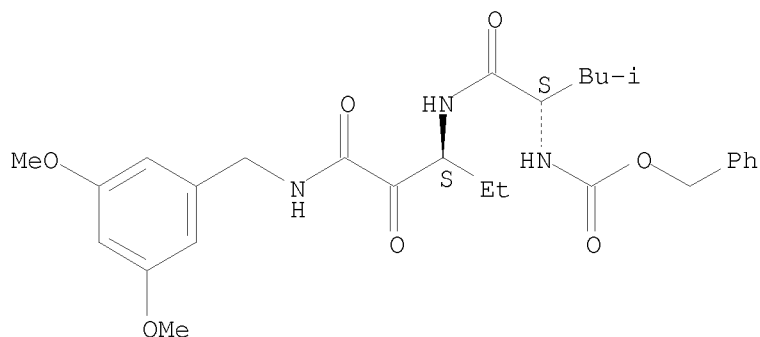
CN	Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)	(CA INDEX NAME)
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Absolute stereochemistry.



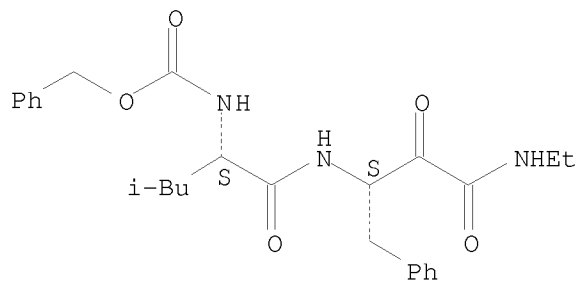
RN 144231-85-6 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144248-93-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

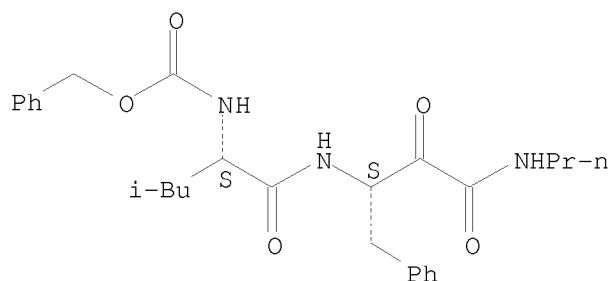
Absolute stereochemistry.



RN 144248-94-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

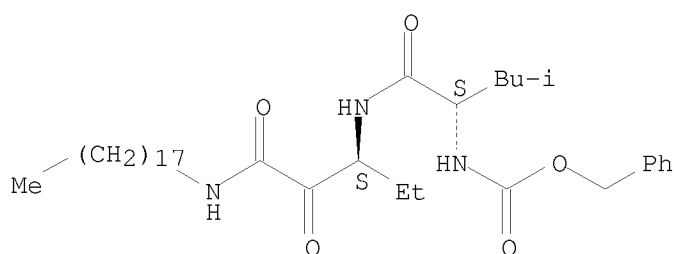




RN 144248-95-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octadecylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

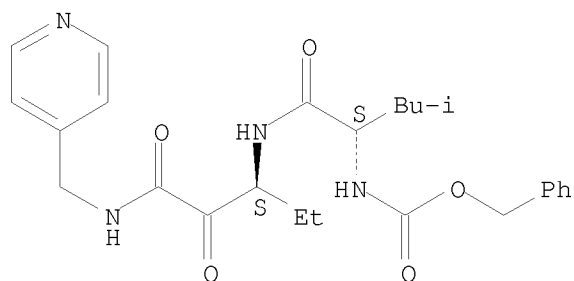
Absolute stereochemistry.



RN 144248-96-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

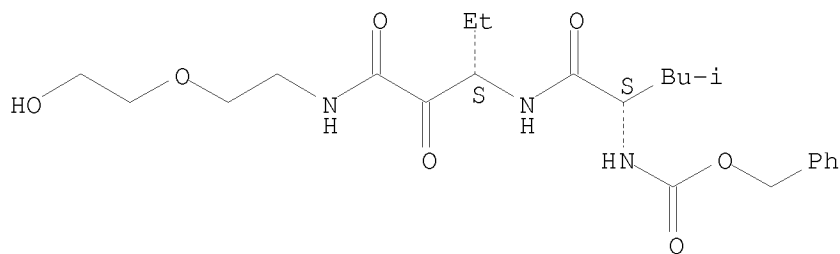
Absolute stereochemistry.



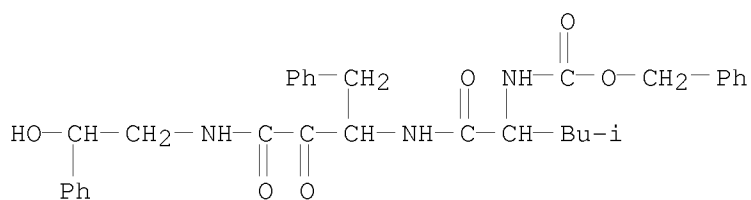
RN 144863-87-6 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid, 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.

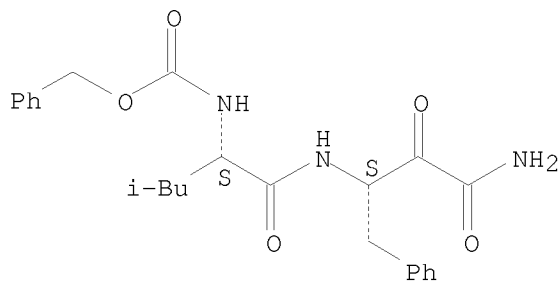


RN 153370-23-1 CAPLUS  
 CN Carbamic acid, [1-[[[3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

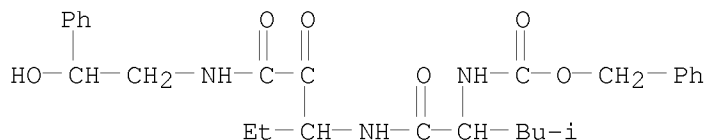


RN 153370-24-2 CAPLUS  
 CN Carbamic acid, [1-[[[3-amino-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



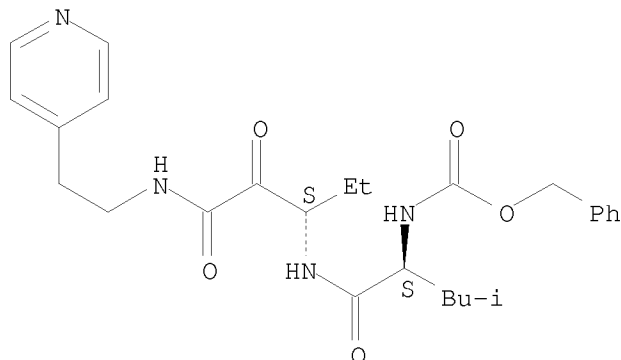
RN 153370-25-3 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-33-3 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2-(4-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

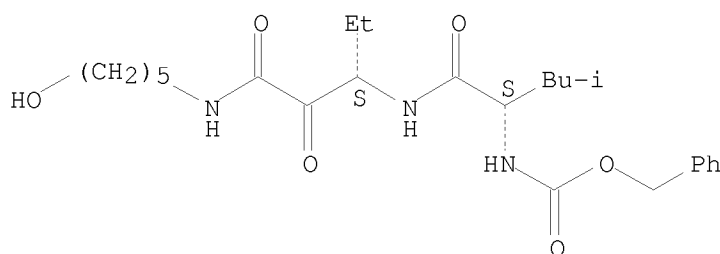
Absolute stereochemistry.



RN 153370-34-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(5-hydroxypentyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

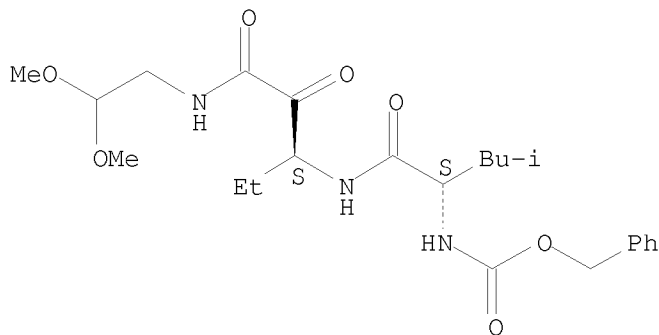
Absolute stereochemistry.



RN 153370-35-5 CAPLUS

CN 2-Oxa-5,9,12-triazatridecan-13-oic acid, 8-ethyl-3-methoxy-11-(2-methylpropyl)-6,7,10-trioxo-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

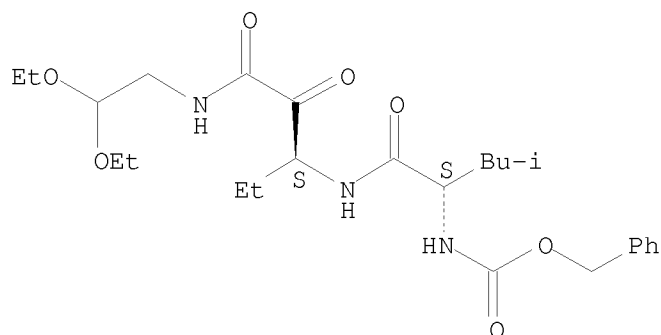
Absolute stereochemistry.



RN 153370-36-6 CAPLUS

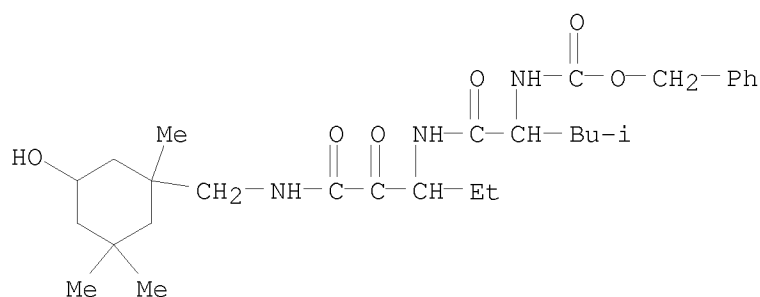
CN 12-Oxa-2,5,9-triazatetradecanoic acid, 11-ethoxy-6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-37-7 CAPLUS

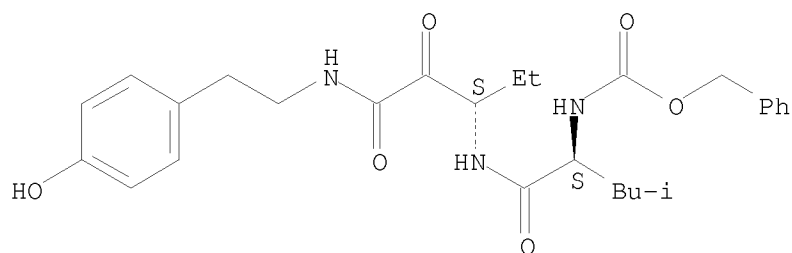
CN Carbamic acid, [1-[[[1-ethyl-3-[[[5-hydroxy-1,3,3-trimethylcyclohexyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-38-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-hydroxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

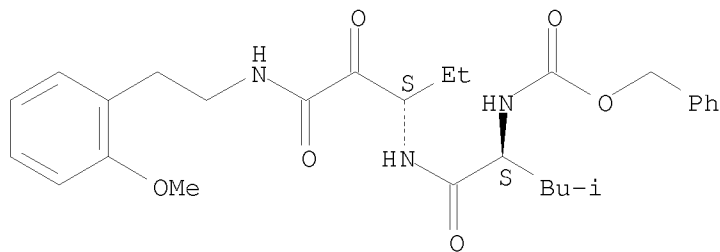
Absolute stereochemistry.



RN 153370-39-9 CAPLUS

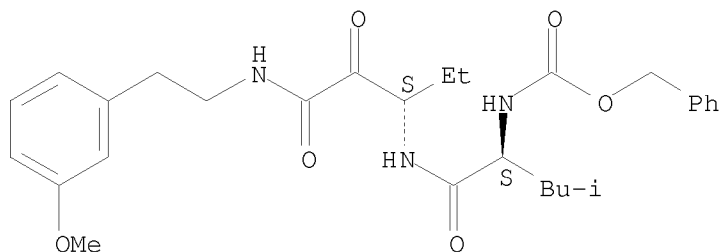
CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(2-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



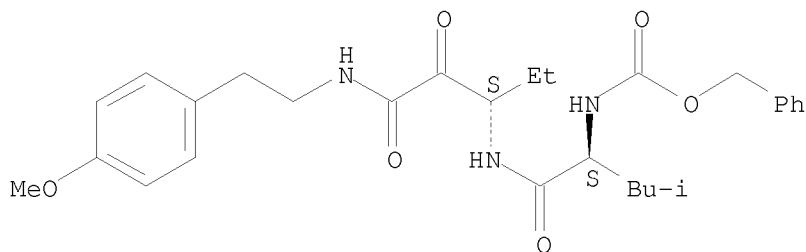
RN 153370-40-2 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(3-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



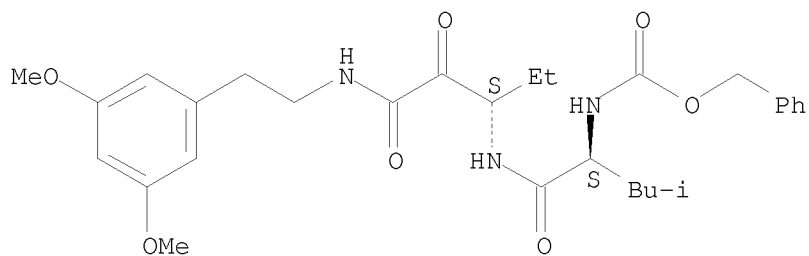
RN 153370-41-3 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



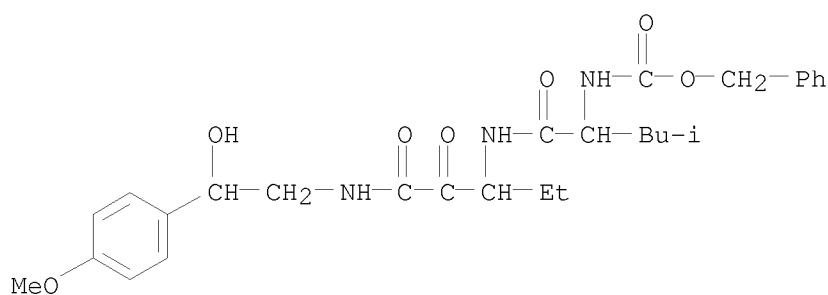
RN 153370-42-4 CAPLUS  
 CN Carbamic acid, [1-[[[3-[[2-(3,5-dimethoxyphenyl)ethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



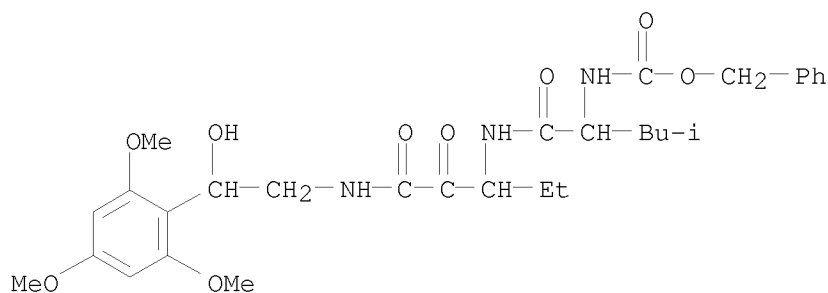
RN 153370-43-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



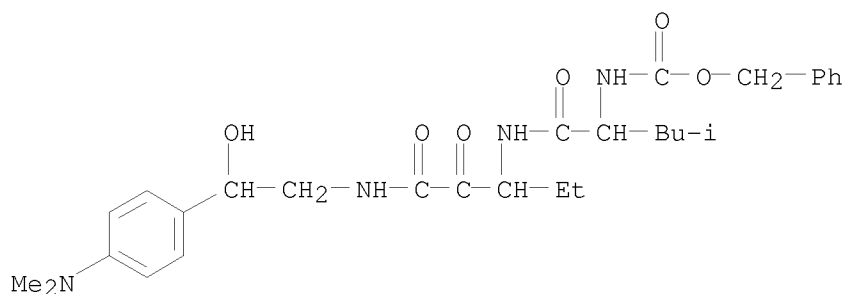
RN 153370-44-6 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(2,4,6-trimethoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



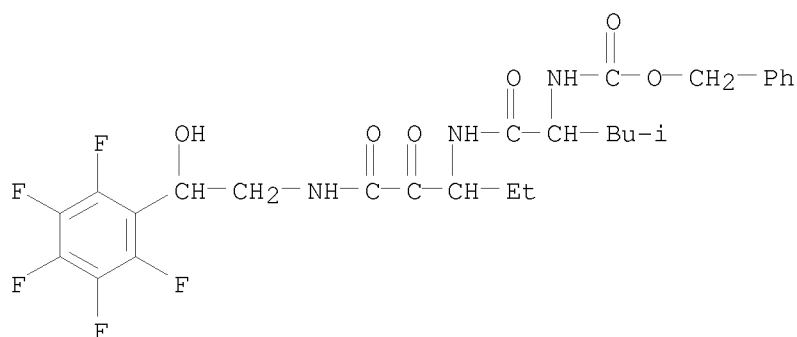
RN 153370-45-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



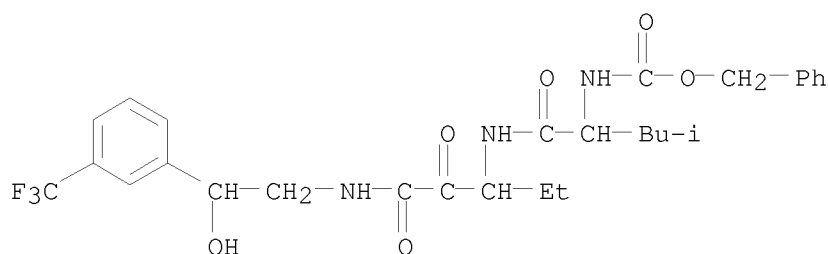
RN 153370-46-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



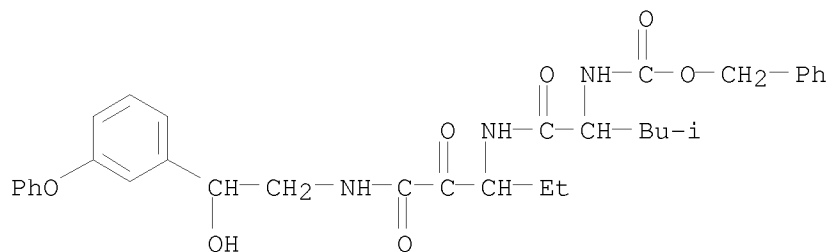
RN 153370-47-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



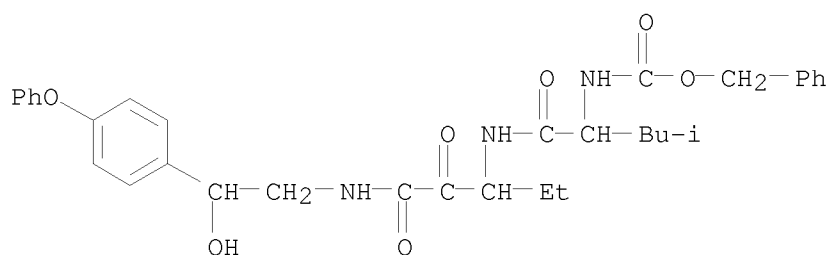
RN 153370-48-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



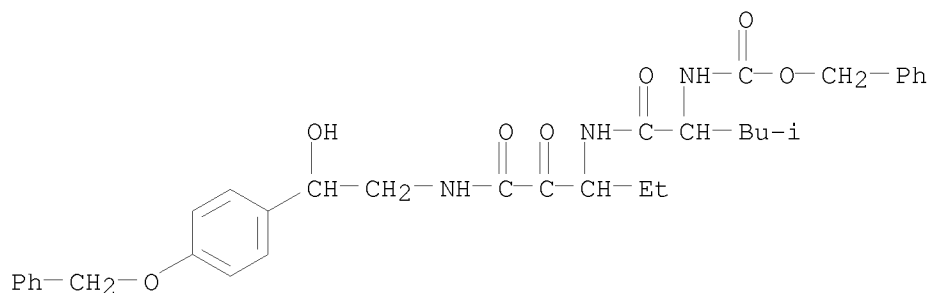
RN 153370-49-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



RN 153370-50-4 CAPLUS

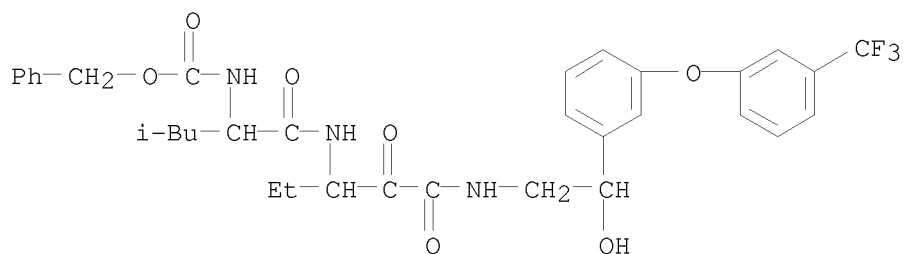
CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-51-5 CAPLUS

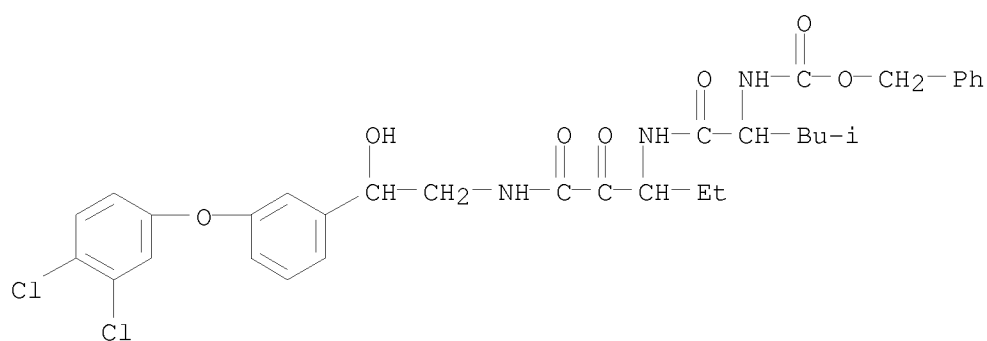
CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)





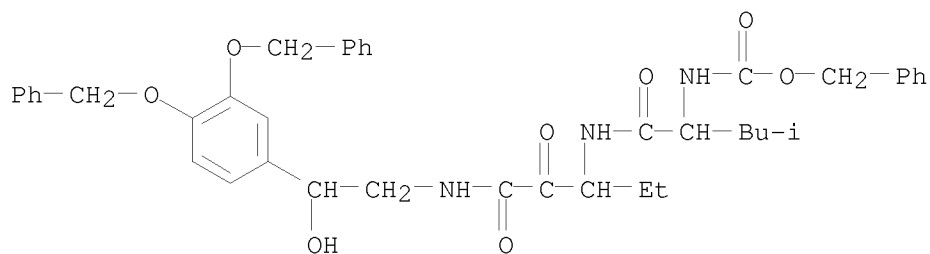
RN 153370-52-6 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



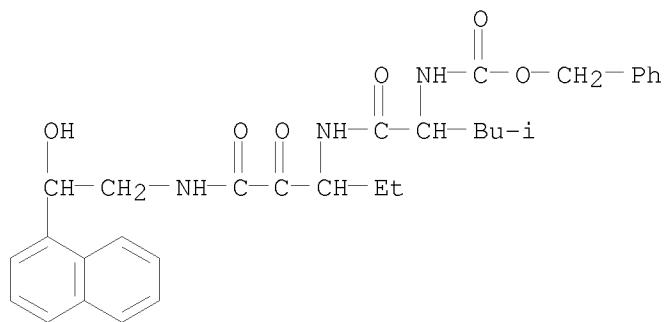
RN 153370-53-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



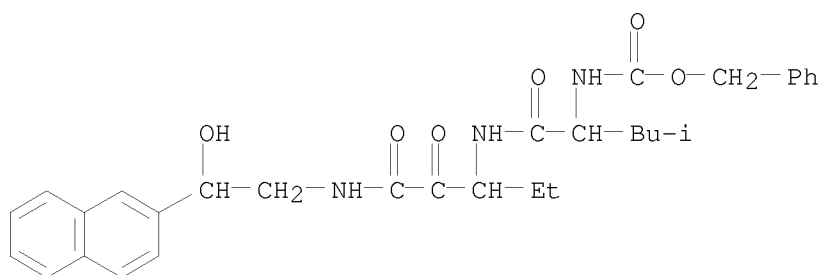
RN 153370-54-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(1-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



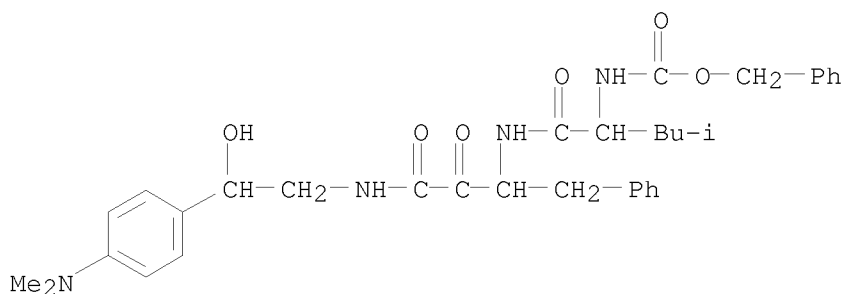
RN 153370-55-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(2-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



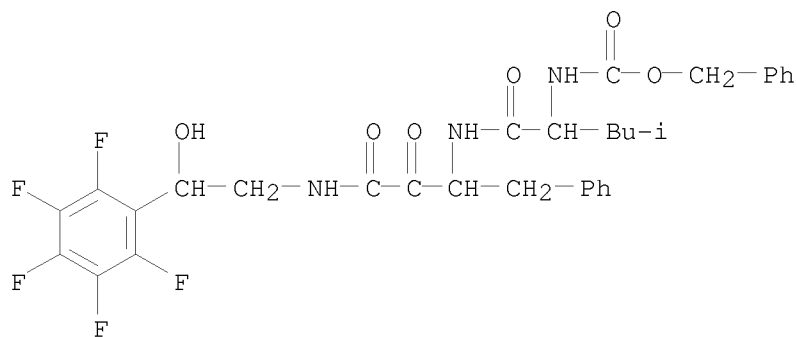
RN 153370-56-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

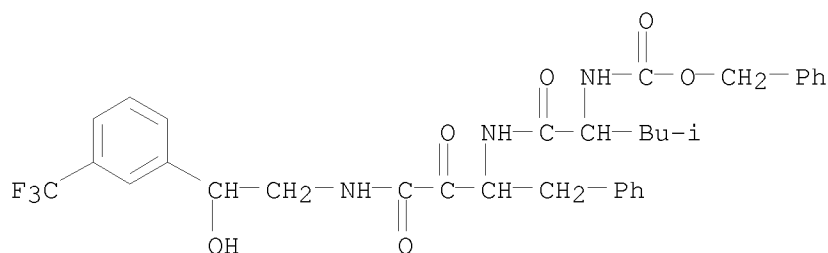


RN 153370-57-1 CAPLUS

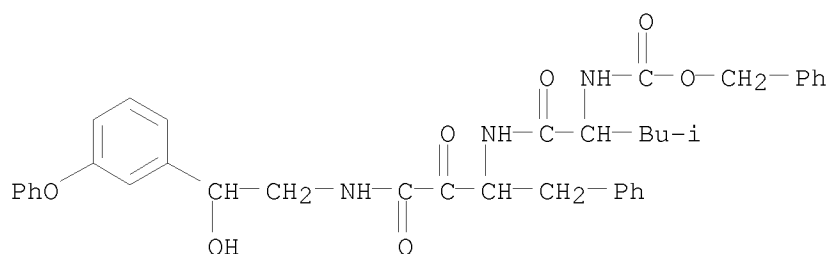
CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



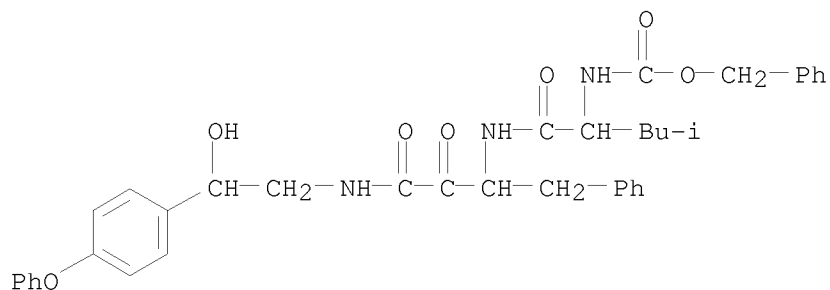
RN 153370-58-2 CAPLUS  
 CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-59-3 CAPLUS  
 CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

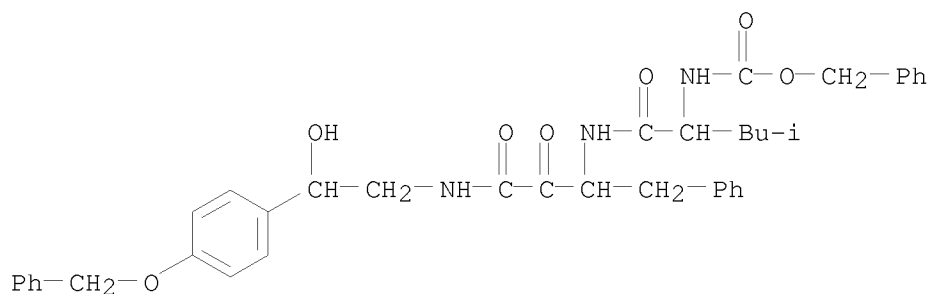


RN 153370-60-6 CAPLUS  
 CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



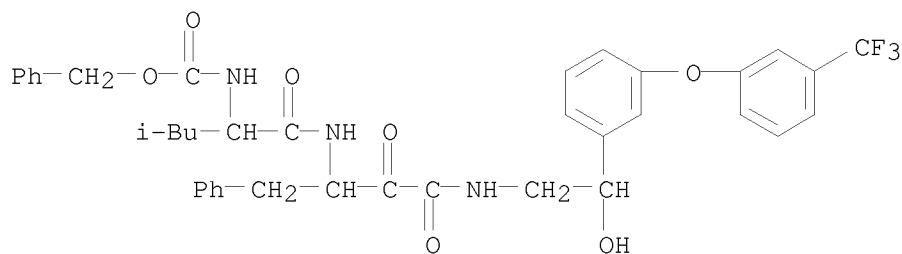
RN 153370-61-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



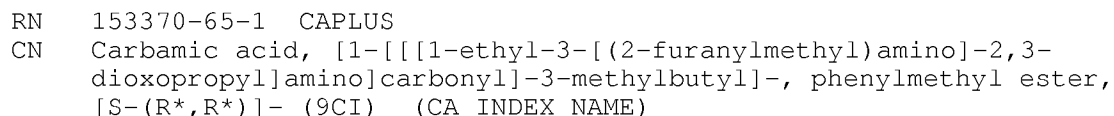
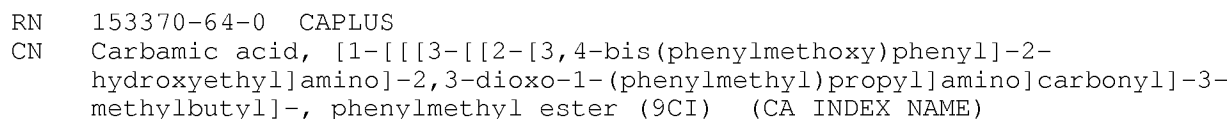
RN 153370-62-8 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-63-9 CAPLUS

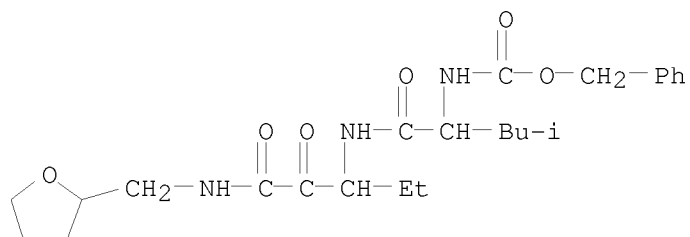
CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



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RN      153370-66-2  CAPLUS
CN      Carbamic acid, [1-[[[1-ethyl-3-[[ (tetrahydro-2-furanyl)methyl]amino]-2,3-
        dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA
        INDEX NAME)

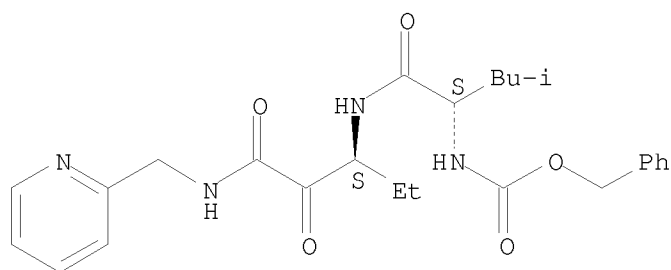
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RN 153370-67-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

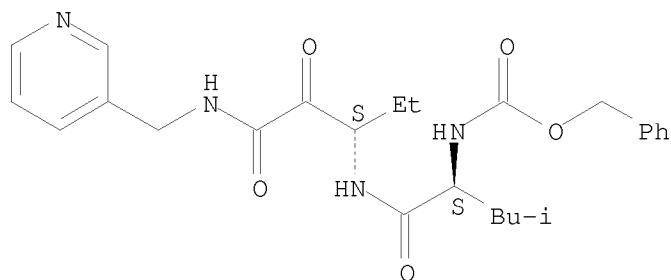
Absolute stereochemistry.



RN 153370-68-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(3-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

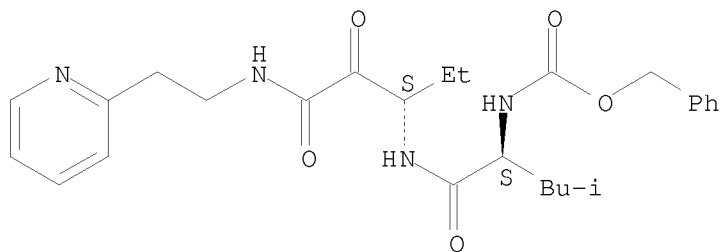
Absolute stereochemistry.



RN 153370-69-5 CAPLUS

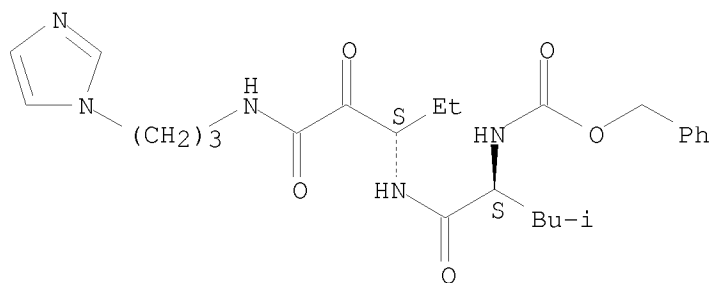
CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2-(2-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



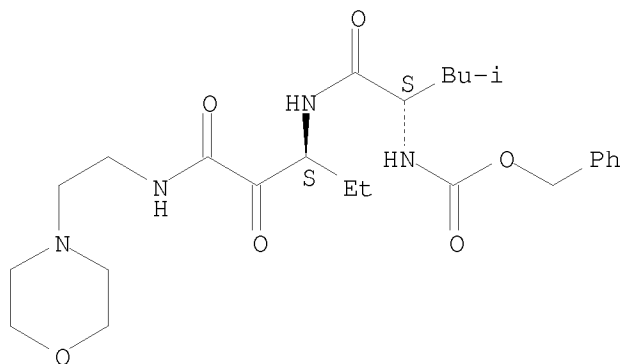
RN 153370-70-8 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[3-(1H-imidazol-1-yl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



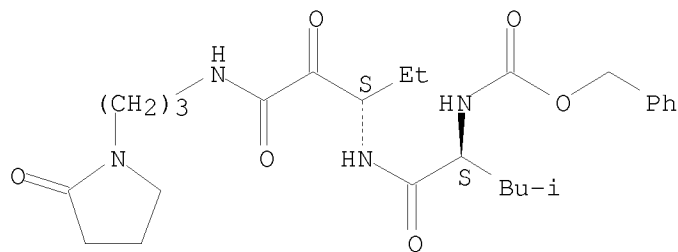
RN 153370-71-9 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-morpholinyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-72-0 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

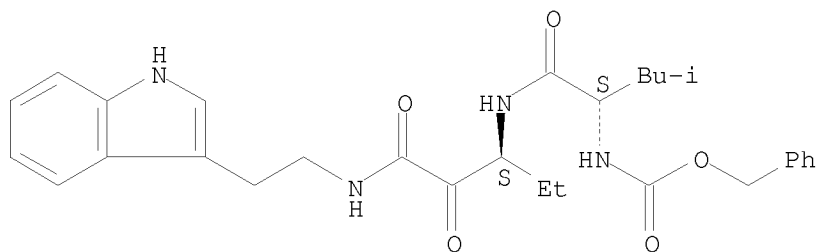
Absolute stereochemistry.



RN 153370-73-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(1H-indol-3-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

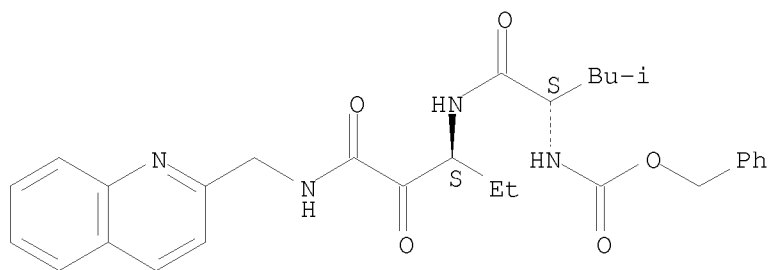
Absolute stereochemistry.



RN 153370-74-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

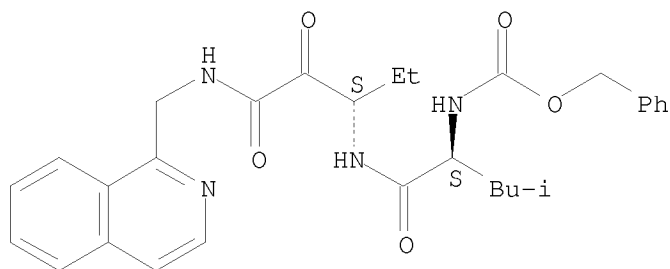


RN 153370-75-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(1-isoquinolinylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

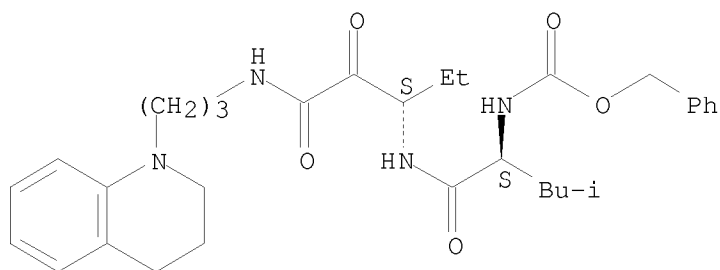




RN 153370-76-4 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

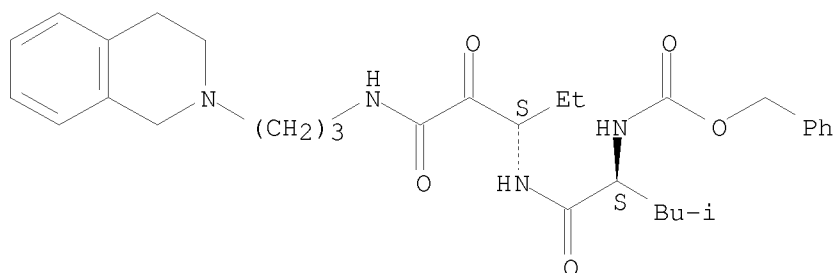
Absolute stereochemistry.



RN 153370-77-5 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

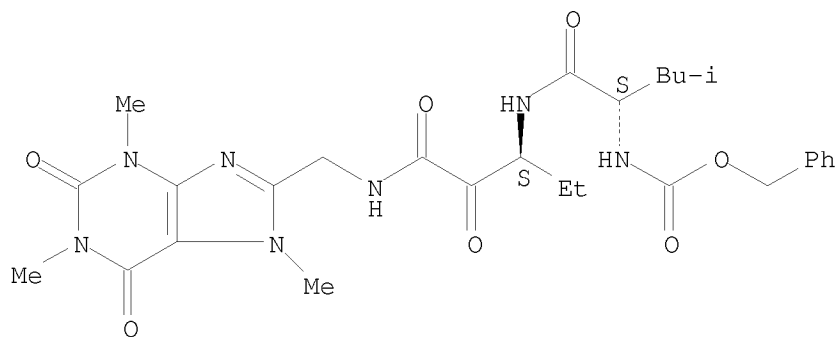
Absolute stereochemistry.



RN 153370-78-6 CAPLUS

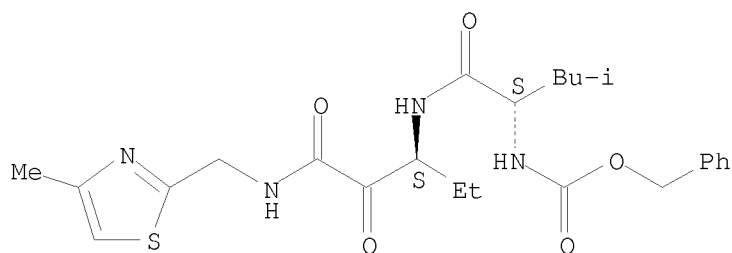
CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



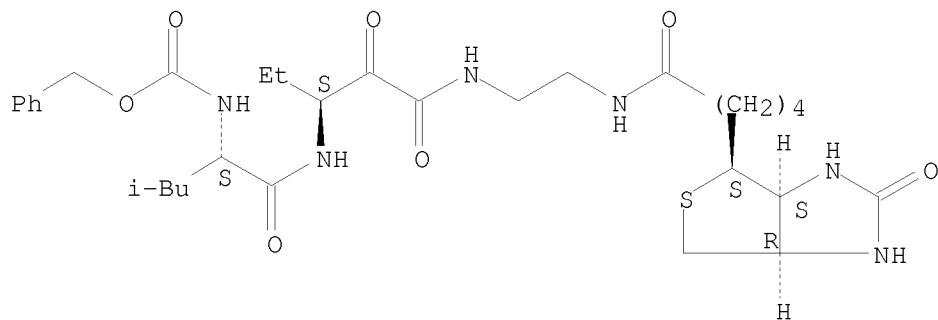
RN 153370-79-7 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[[4-methyl-2-thiazolyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



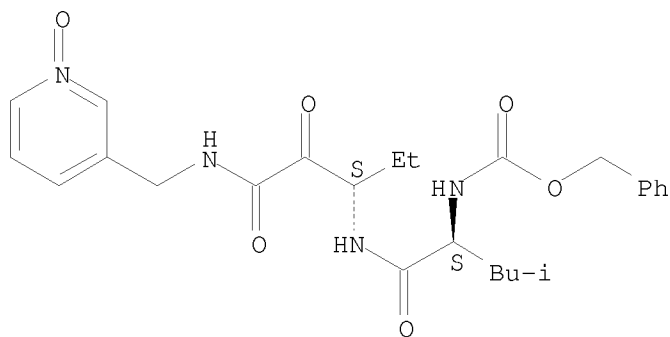
RN 153370-80-0 CAPLUS  
 CN 2,5,9,12-Tetraazaheptadecanoic acid, 6-ethyl-17-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-3-(2-methylpropyl)-4,7,8,13-tetraoxo-, phenylmethyl ester, [3aS-[3aα,4β(3R\*,6R\*),6aα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-81-1 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[[1-oxido-3-pyridinyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

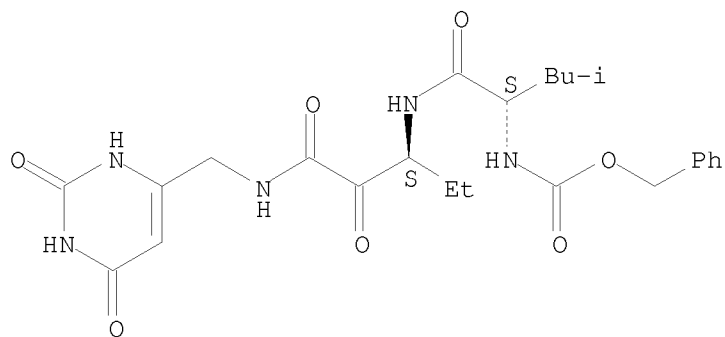
Absolute stereochemistry.



RN 153370-82-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

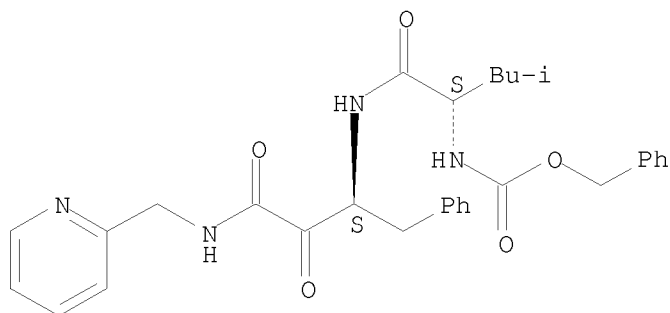
Absolute stereochemistry.



RN 153370-83-3 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

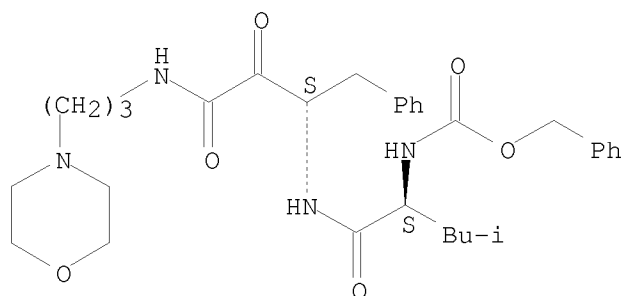
Absolute stereochemistry.



RN 153370-84-4 CAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

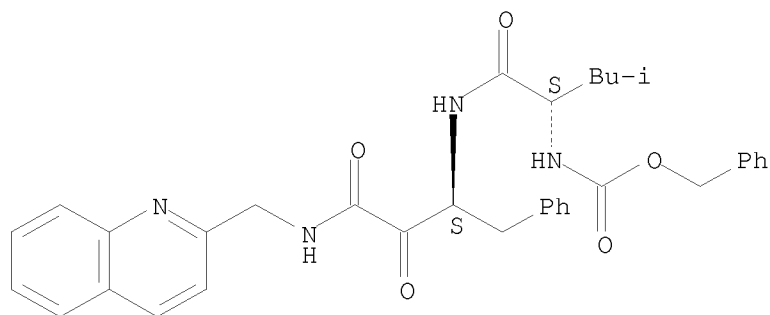
Absolute stereochemistry.



RN 153370-85-5 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

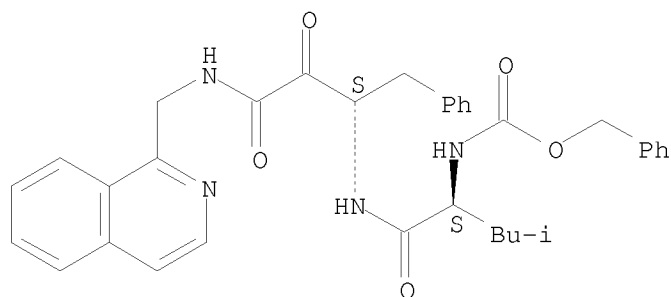
Absolute stereochemistry.



RN 153370-86-6 CAPLUS

CN Carbamic acid, [1-[[[3-[(1-isoquinolinylmethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

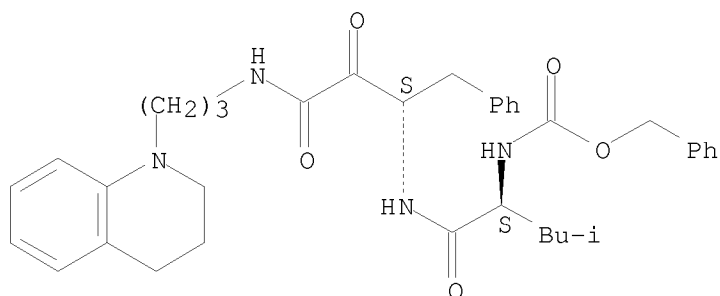
Absolute stereochemistry.



RN 153370-87-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

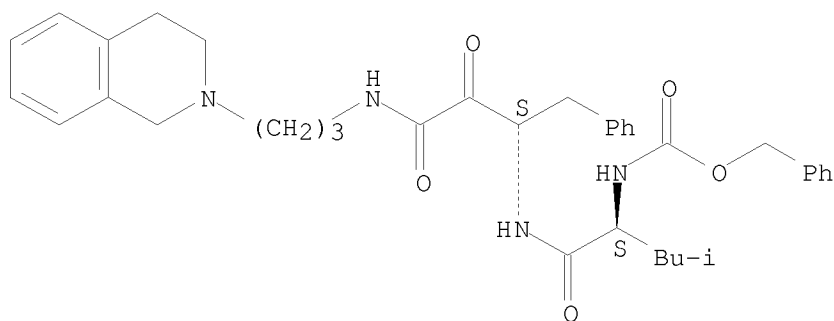
Absolute stereochemistry.



RN 153370-88-8 CAPLUS

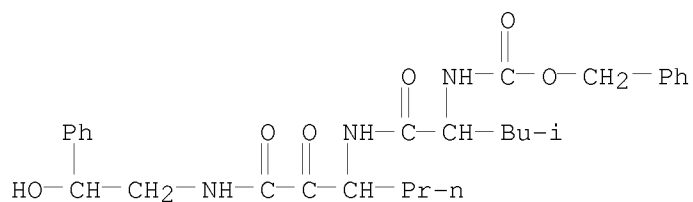
CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-89-9 CAPLUS

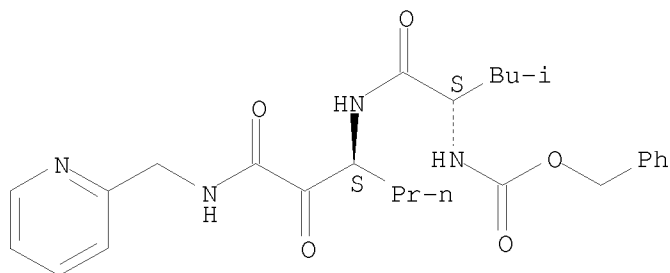
CN Carbamic acid, [1-[[[1-[[[(2-hydroxy-2-phenylethyl)amino]oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-90-2 CAPLUS

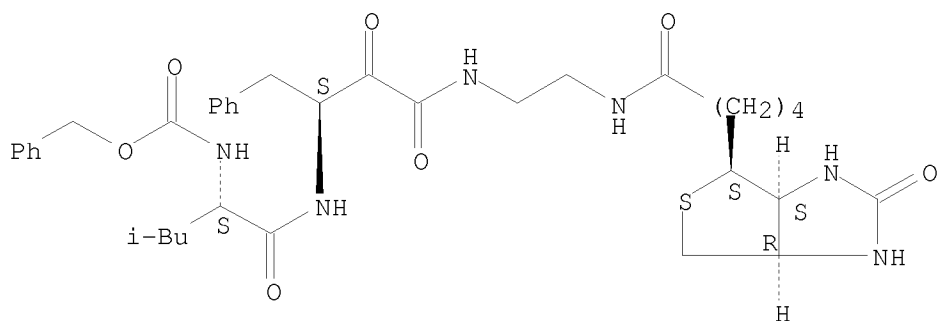
CN Carbamic acid, [3-methyl-1-[[[1-[oxo[(2-pyridinylmethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



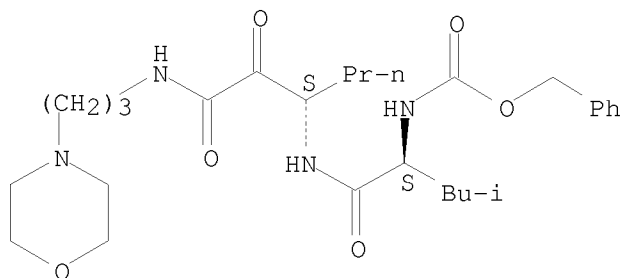
RN 153370-91-3 CAPLUS  
 CN 2,5,9,12-Tetraazaheptadecanoic acid,  
 17-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-3-(2-methylpropyl)-  
 4,7,8,13-tetraoxo-6-(phenylmethyl)-, phenylmethyl ester,  
 [3aS-[3αα,4β(3R\*,6R\*),6αα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



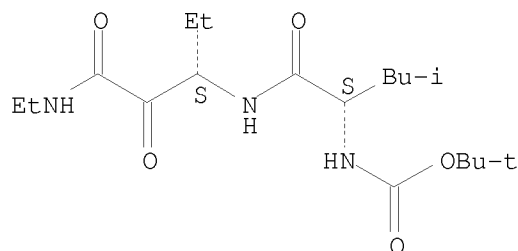
RN 153370-92-4 CAPLUS  
 CN Carbamic acid, [3-methyl-1-[[[1-[[[3-(4-morpholinyl)propyl]amino]oxoacetyl]butyl]amino]carbonyl]butyl]-,  
 phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153371-08-5 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester,  
 [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1993:644174 CAPLUS

DOCUMENT NUMBER: 119:244174

ORIGINAL REFERENCE NO.: 119:43411a, 43414a

TITLE: Peptide  $\alpha$ -keto ester,  $\alpha$ -keto amide, and  $\alpha$ -keto acid inhibitors of calpains and other cysteine proteases

AUTHOR(S): Li, Zhaozhao; Patil, Girish S.; Golubski, Zbigniew E.; Hori, Hitoshi; Tehrani, Kamin; Foreman, J. E.; Eveleth, David D.; Bartus, Raymond T.; Powers, James C.

CORPORATE SOURCE: Sch. Chem. Biochem., Georgia Inst. Technol., Atlanta, GA, 30332-0400, USA

SOURCE: Journal of Medicinal Chemistry (1993), 36(22), 3472-80

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of dipeptidyl and tripeptidyl  $\alpha$ -keto esters,  $\alpha$ -keto amides, and  $\alpha$ -keto acids having leucine in the P2 position were synthesized and evaluated as inhibitors for the cysteine proteases calpain I, calpain II, cathepsin B, and papain. In general, peptidyl  $\alpha$ -keto acids, were more inhibitory toward calpain I and II than  $\alpha$ -keto amides, which in turn were more effective than  $\alpha$ -keto esters. In the series Z-Leu-AA-COOEt, the inhibitory potency decreased in the order: Met (lowest KI) > Nva > Phe > 4-Cl-Phe > Abu > Nle (highest KI) with calpain I, while almost the reverse order was observed for calpain II. Extending the dipeptide  $\alpha$ -keto ester to a tripeptide  $\alpha$ -keto ester yielded significant enhancement in the inhibitory potency toward cathepsin B, but smaller changes toward the calpains. Changing the ester group in the  $\alpha$ -keto esters did not substantially decrease KI values for calpain I and calpain II. N-monosubstituted  $\alpha$ -keto amides were better inhibitors than the corresponding  $\alpha$ -keto esters.  $\alpha$ -Keto amides with hydrophobic alkyl groups or alkyl groups with an attached Ph group had the lower KI values. N,N-disubstituted  $\alpha$ -keto amides were much less potent inhibitors than the corresponding N-monosubstituted peptide  $\alpha$ -keto amides. The peptide  $\alpha$ -keto acid Z-Leu-Phe-COOH was the best inhibitor for calpain I (KI = 0.0085  $\mu$ M) and calpain II (KI = 0.0057  $\mu$ M) discovered in this study. It is likely that the inhibitors are transition-state analogs and form tetrahedral adducts with the active site cysteine of cysteine proteases and form hydrogen bonds with the active site histidine and possibly another hydrogen bond donor in the case of monosubstituted amides. Several inhibitors prevented spectrin degradation in a platelet membrane permeability assay and may be useful for the treatment of diseases which involve neurodegeneration.

IT 150519-08-7P 150519-09-8P 150519-12-3P  
150519-18-9P 150519-19-0P 150519-20-3P  
150957-45-2P 150957-46-3P 150957-49-6P

150957-50-9P

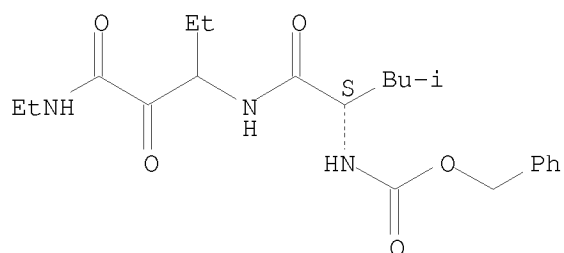
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and cysteine proteinase inhibition by and platelet membrane permeability of)

RN 150519-08-7 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

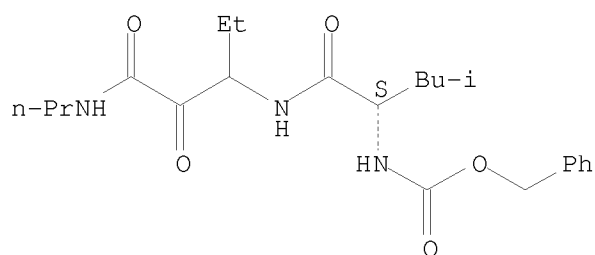
Absolute stereochemistry.



RN 150519-09-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

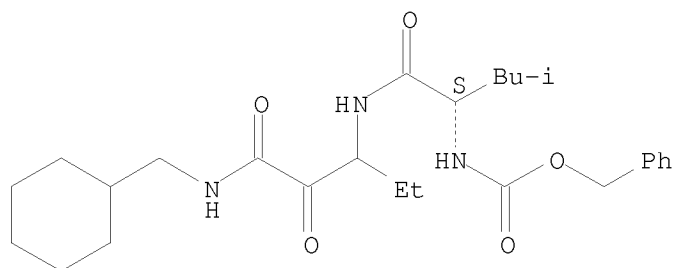
Absolute stereochemistry.



RN 150519-12-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-[(cyclohexylmethyl)amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



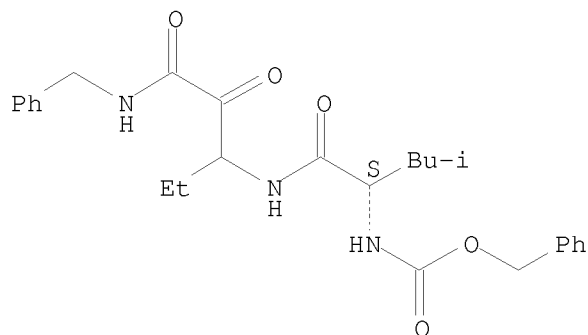
RN 150519-18-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl



ester (9CI) (CA INDEX NAME)

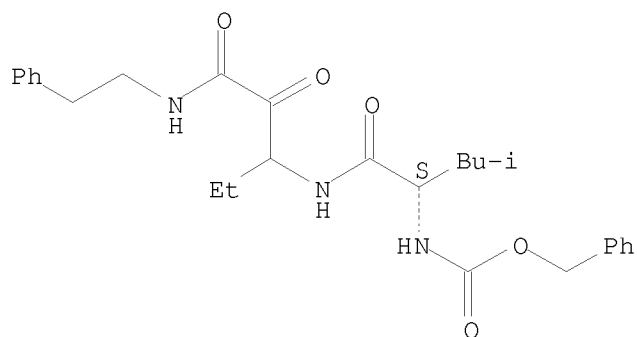
Absolute stereochemistry.



RN 150519-19-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

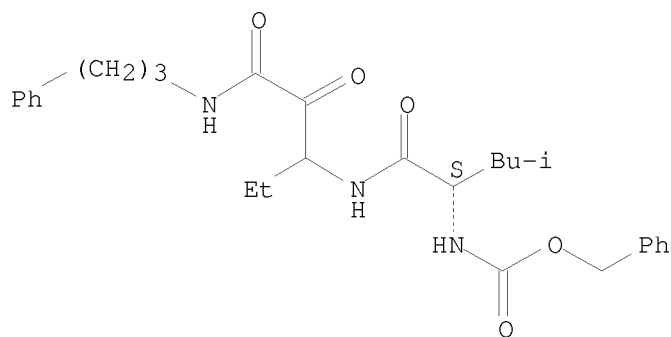
Absolute stereochemistry.



RN 150519-20-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[1-ethyl-2,3-dioxo-3-[(3-phenylpropyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

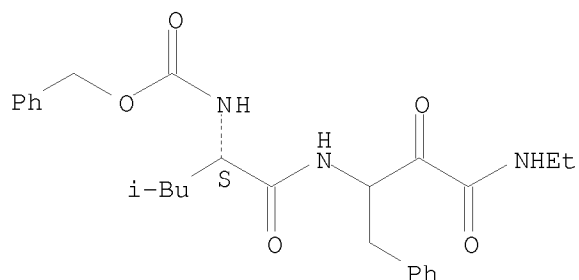


RN 150957-45-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-(ethylamino)-2,3-dioxo-1-

(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

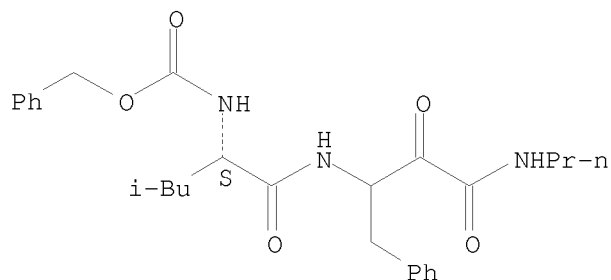
Absolute stereochemistry.



RN 150957-46-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

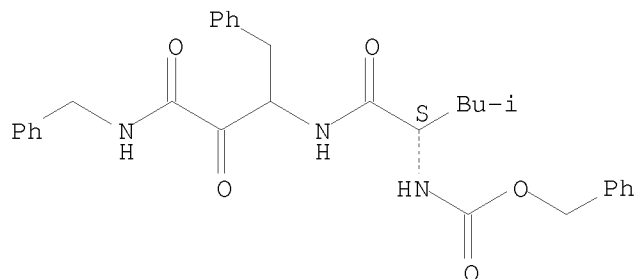
Absolute stereochemistry.



RN 150957-49-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

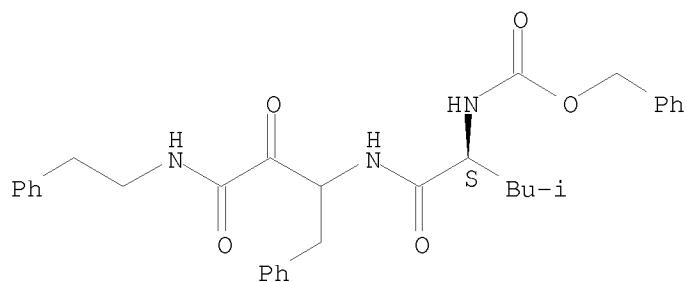
Absolute stereochemistry.



RN 150957-50-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1993:81438 CAPLUS  
DOCUMENT NUMBER: 118:81438  
ORIGINAL REFERENCE NO.: 118:14353a,14356a  
TITLE: Peptide keto amides, keto acids, and keto esters  
INVENTOR(S): Powers, James C.  
PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA  
SOURCE: PCT Int. Appl., 89 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9212140	A1	19920723	WO 1991-US9801	19911227 <--
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2098702	A1	19920629	CA 1991-2098702	19911227 <--
AU 9191553	A	19920817	AU 1991-91553	19911227 <--
AU 654834	B2	19941124		
EP 564561	A1	19931013	EP 1992-903265	19911227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL				
PRIORITY APPLN. INFO.:			US 1990-635287	A 19901228 <--
			WO 1991-US9801	A 19911227 <--

OTHER SOURCE(S): MARPAT 118:81438

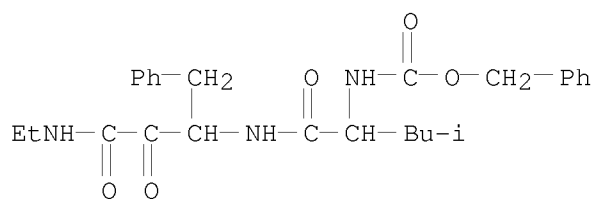
AB Title compds. R-X-X1-COR1 [X, X1 = amino acids; R = H, (un)substituted H2NCO, H2NCS, H2NSO2, amino acid; R1 = alkoxy, OH, (un)substituted NH2] were prepared as serine and cysteine protease inhibitors. Thus, Z-Leu-Phe-OH (Z = CO2CH2Ph) was treated with ClCOCO2Et in the presence of 4-dimethylaminopyridine to give Z-Leu-NHC(CH2Ph)=C(CO2Et)O2CCO2Et which was hydrolyzed to 2-Leu-Phe-CO2Et. The latter compound was ketalized and amidated with EtNH2, to give Z-Leu-Phe-CONHET (I). I inhibited calpain from humor erythrocytes at 7  $\mu$ m.

IT 145731-36-8P 145731-38-0P 145731-39-1P  
145731-40-4P 145731-41-5P 145731-42-6P  
145731-43-7P 145731-44-8P 145731-45-9P  
145731-46-0P 145731-47-1P 145731-48-2P  
145731-49-3P 145731-50-6P 145731-51-7P  
145731-52-8P 145731-53-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and protease-inhibiting activity of)

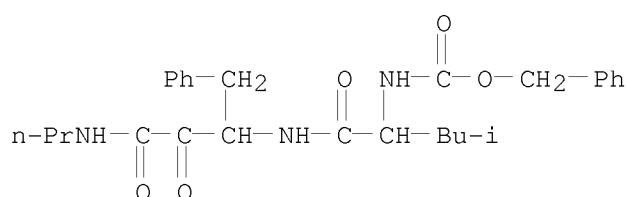
RN 145731-36-8 CAPLUS

CN Carbamic acid, [1-[[[3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



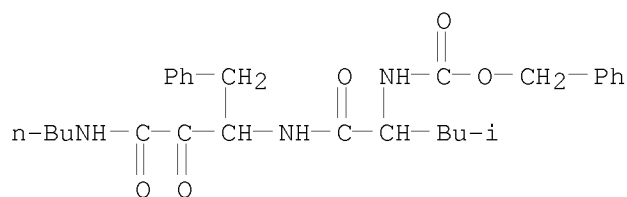
RN 145731-38-0 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



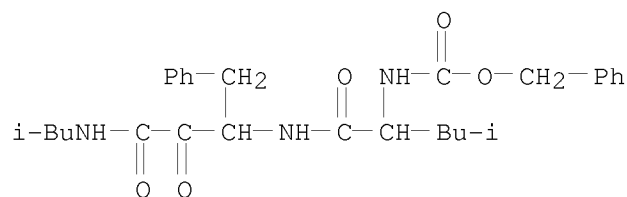
RN 145731-39-1 CAPLUS

CN Carbamic acid, [1-[[[3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



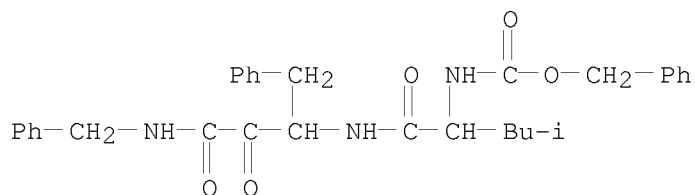
RN 145731-40-4 CAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-[(2-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



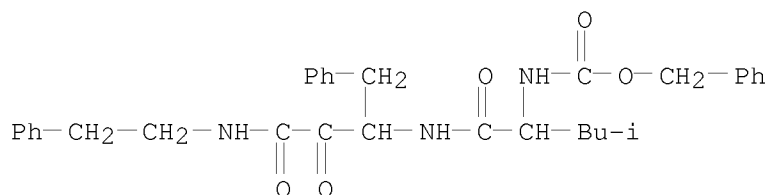
RN 145731-41-5 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



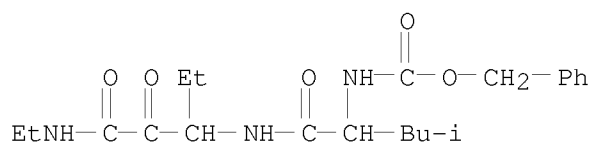
RN 145731-42-6 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



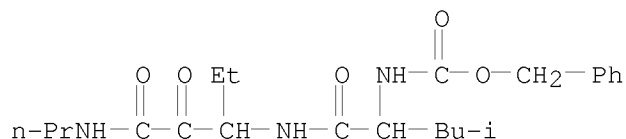
RN 145731-43-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



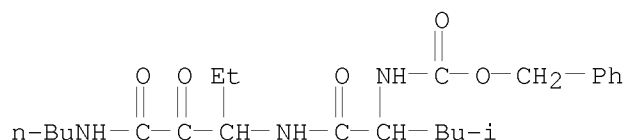
RN 145731-44-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

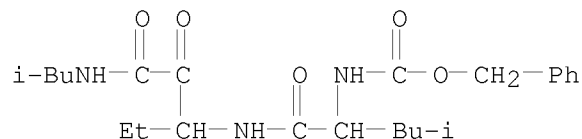


RN 145731-45-9 CAPLUS

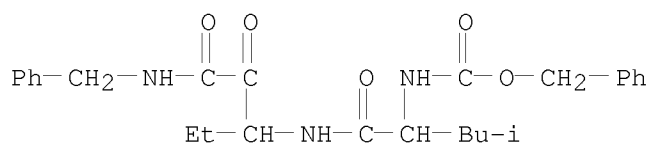
CN Carbamic acid, [1-[[[3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



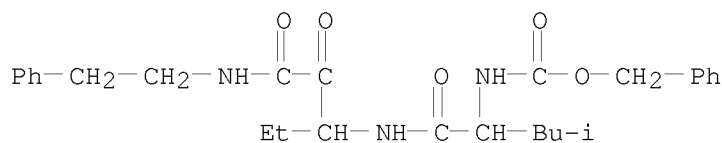
RN 145731-46-0 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



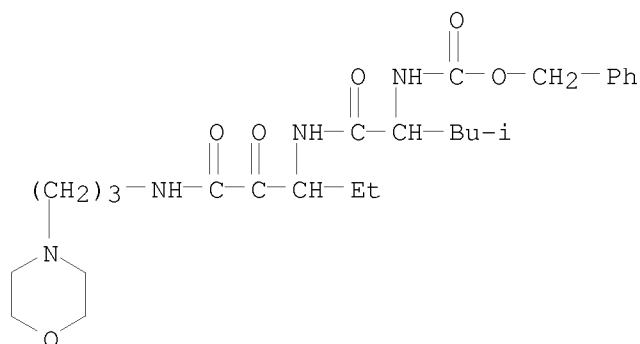
RN 145731-47-1 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 145731-48-2 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

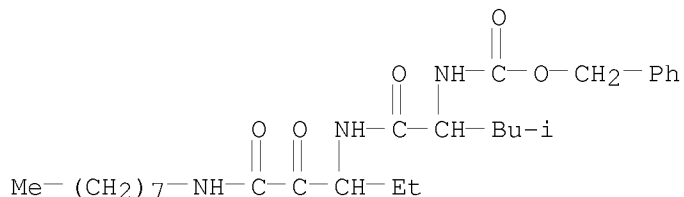


RN 145731-49-3 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



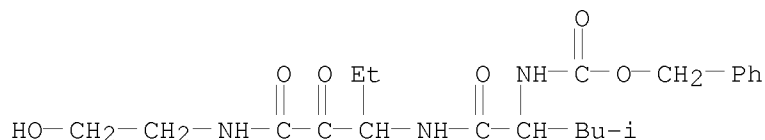
RN 145731-50-6 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-(octylamino)-2,3-

dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA  
INDEX NAME)



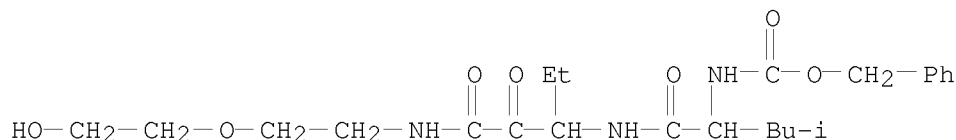
RN 145731-51-7 CAPLUS

CN	Carbamic acid, [1-[[[1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)	(CA INDEX NAME)
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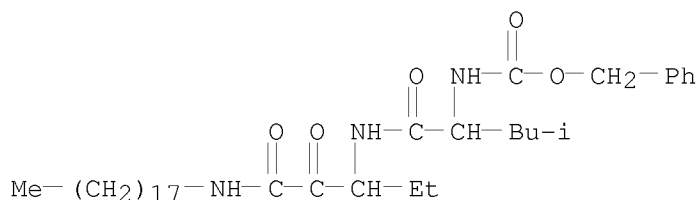
RN 145731-52-8 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid,  
6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester  
(CA INDEX NAME)



RN 145731-53-9 CAPLUS

CN	Carbamic acid, [1-[[[1-ethyl-3-(octadecylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)
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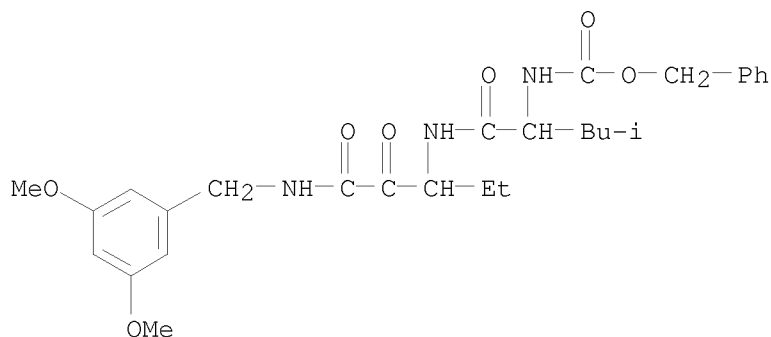


IT 145731-54-0P 145731-55-1P

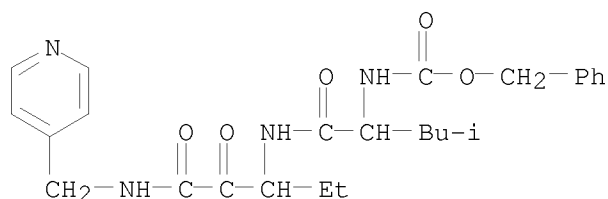
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 145731-54-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 145731-55-1 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1993:822 CAPLUS  
 DOCUMENT NUMBER: 118:822  
 ORIGINAL REFERENCE NO.: 118:171a,174a  
 TITLE: Use of calpain inhibitors in the inhibition and treatment of neurodegeneration  
 INVENTOR(S): Bartus, Raymond T.; Eveleth, David D., Jr.; Lynch, Gary S.; Powers, James C.  
 PATENT ASSIGNEE(S): Cortex Pharmaceuticals, Inc., USA; Georgia Tech Research Corp.  
 SOURCE: PCT Int. Appl., 133 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9211850	A2	19920723	WO 1991-US9786	19911227 <--
WO 9211850	A3	19920903		
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2098609	A1	19920629	CA 1991-2098609	19911227 <--
AU 9191527	A	19920817	AU 1991-91527	19911227 <--
AU 667463	B2	19960328		
EP 564552	A1	19931013	EP 1992-902904	19911227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06504061	T	19940512	JP 1991-503767	19911227 <--



US 5444042	A	19950822	US 1994-207881	19940307 <--
AU 9655905	A	19960822	AU 1996-55905	19960611 <--
AU 9923782	A	19990603	AU 1999-23782	19990415 <--
PRIORITY APPLN. INFO.:			US 1990-635952	A 19901228 <--
			US 1991-682925	B2 19910409 <--
			US 1991-816120	B1 19911227 <--
			WO 1991-US9786	A 19911227 <--
			AU 1996-55905	A3 19960611 <--

OTHER SOURCE(S):            MARPAT 118:822

AB    Calpain inhibitors such as isocoumarins, substituted heterocyclic compds., and peptide keto compds., are used in the treatment of neurodegeneration. Examples are given for the synthesis of a large number of these compds. Data are also given showing protease inhibition by halo-ketone peptides, inhibition of calpain in crude brain exts. by calpain inhibitors, in vivo protection against neurodegeneration, membrane permeation of calpain inhibitors, screens for inhibition of anoxic damage, and protection against spectrin breakdown from excitotoxic damage by peripherally administered calpain inhibitors. A neuroprotective composition for i.v. drip was prepared containing Z-Leu-Phe-CONH<sub>2</sub>.

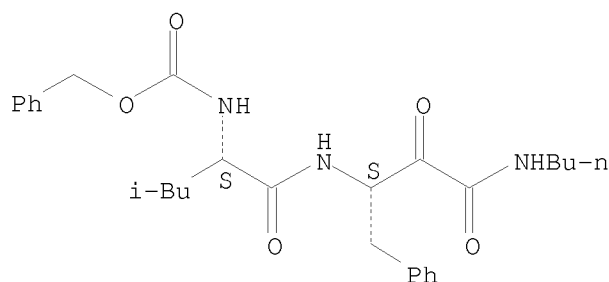
IT    144231-72-1P 144231-73-2P 144231-74-3P  
 144231-75-4P 144231-76-5P 144231-77-6P  
 144231-78-7P 144231-79-8P 144231-80-1P  
 144231-81-2P 144231-82-3P 144231-83-4P  
 144231-84-5P 144231-85-6P 144248-93-1P  
 144248-94-2P 144248-95-3P 144248-96-4P  
 144863-87-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as calpain inhibitor in treatment of neurodegeneration)

RN    144231-72-1    CAPLUS

CN    Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)    (CA INDEX NAME)

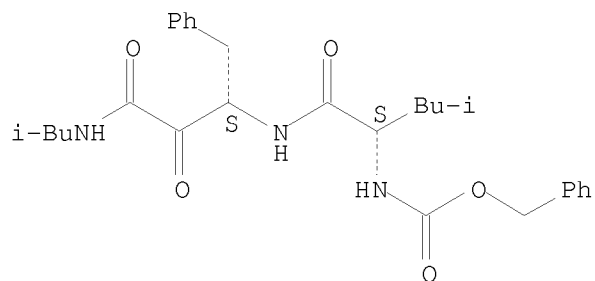
Absolute stereochemistry.



RN    144231-73-2    CAPLUS

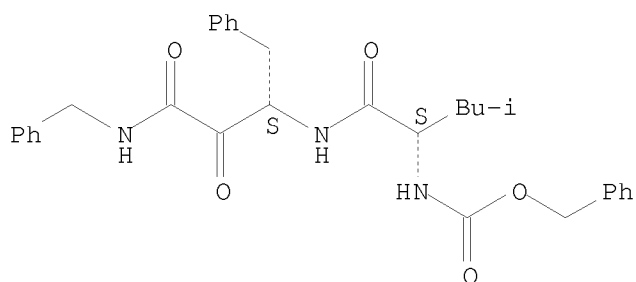
CN    Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-[(2-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI)    (CA INDEX NAME)

Absolute stereochemistry.



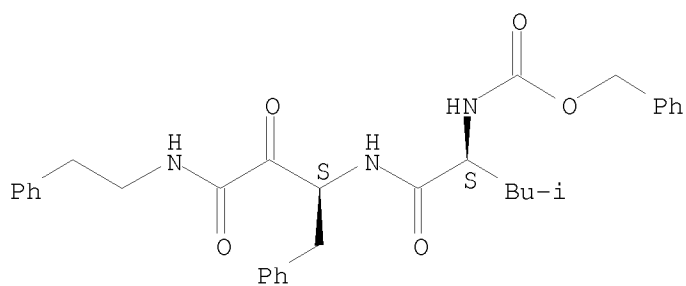
RN 144231-74-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



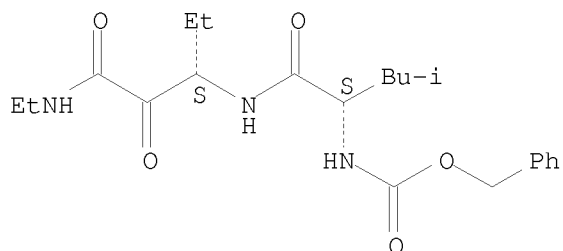
RN 144231-75-4 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



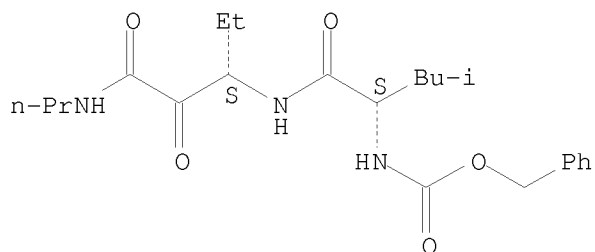
RN 144231-76-5 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



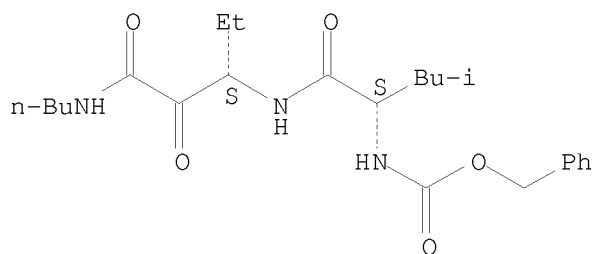
RN 144231-77-6 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



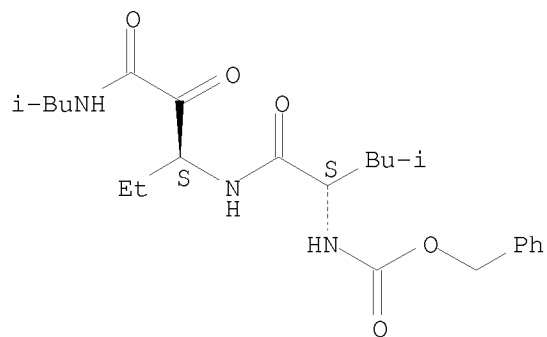
RN 144231-78-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



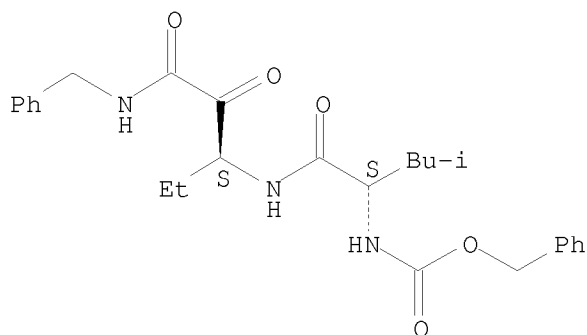
RN 144231-79-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



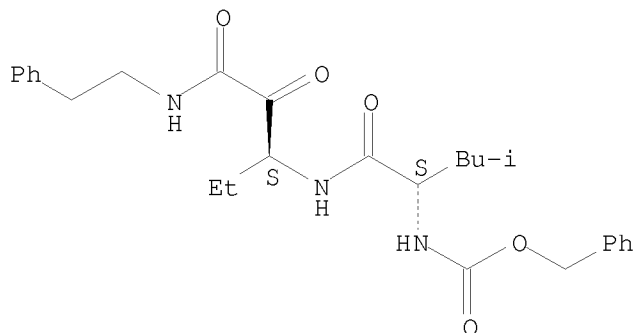
RN 144231-80-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



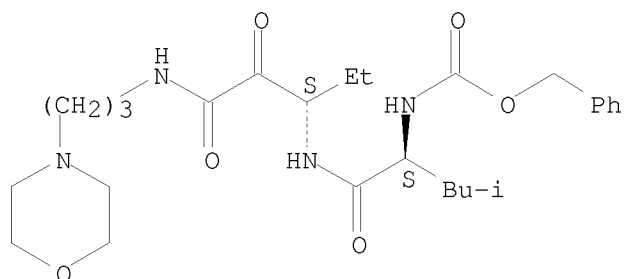
RN 144231-81-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144231-82-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

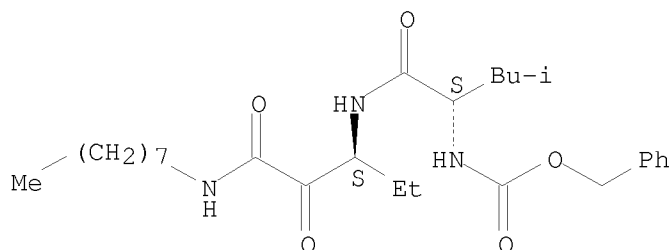
Absolute stereochemistry.



RN 144231-83-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

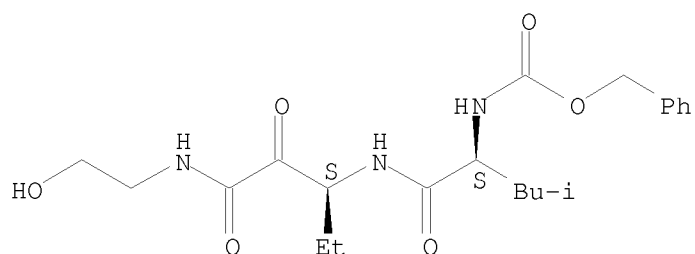
Absolute stereochemistry.



RN 144231-84-5 CAPLUS

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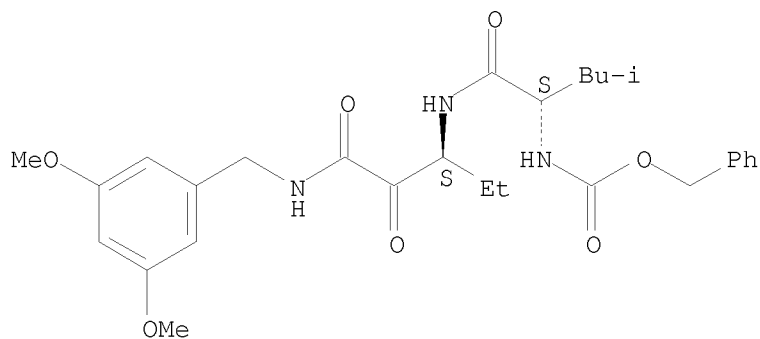
Absolute stereochemistry.



RN 144231-85-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

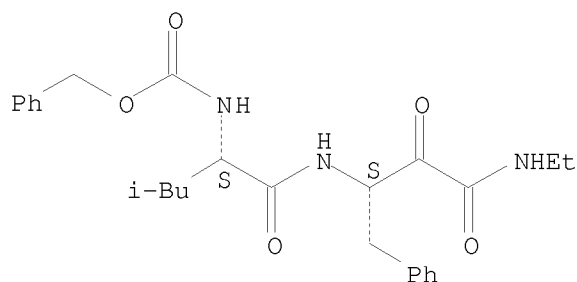
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

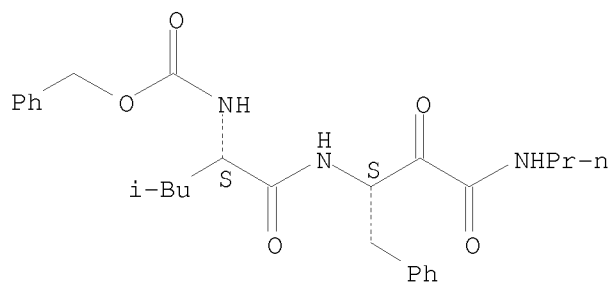
Absolute stereochemistry.



RN 144248-94-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

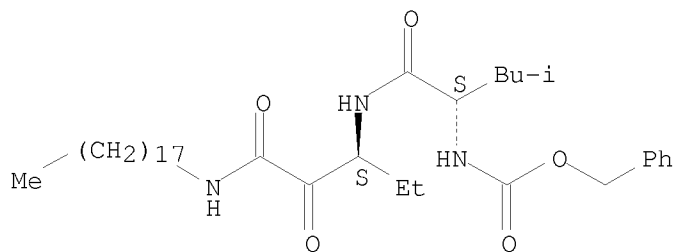
Absolute stereochemistry.



RN 144248-95-3 CAPLUS

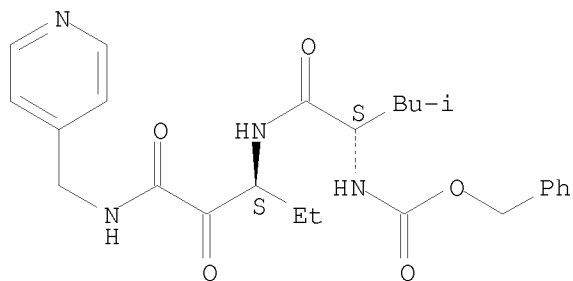
CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octadecylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



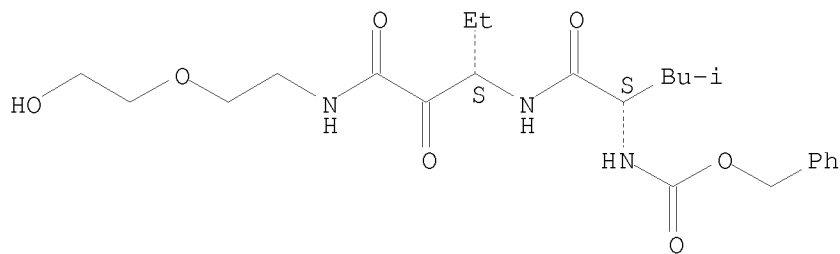
RN 144248-96-4 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144863-87-6 CAPLUS  
 CN 12-Oxa-2,5,9-triazatetradecanoic acid, 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



=> fil stng		
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	254.43	433.00
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-31.20	-31.20

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Nov 21, 2008 (20081121/UP).

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.20	434.20
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CA SUBSCRIBER PRICE	0.00	-31.20

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DICTIONARY FILE UPDATES: 2 DEC 2008 HIGHEST RN 1078799-92-4

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(FILE 'HOME' ENTERED AT 15:40:27 ON 03 DEC 2008)

FILE 'REGISTRY' ENTERED AT 15:40:32 ON 03 DEC 2008

L1 STRUCTURE UPLOADED  
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L3 291 S L1 FULL

FILE 'CAPLUS' ENTERED AT 15:40:57 ON 03 DEC 2008

L4 51 S L3  
L5 1 S US 20070004643 A1/PN  
L6 27 S L4 NOT PATENT/DT  
L7 17 S L6 AND PD<20041208  
L8 24 S L4 NOT L6  
L9 22 S L8 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)  
L10 39 S L7 OR L9

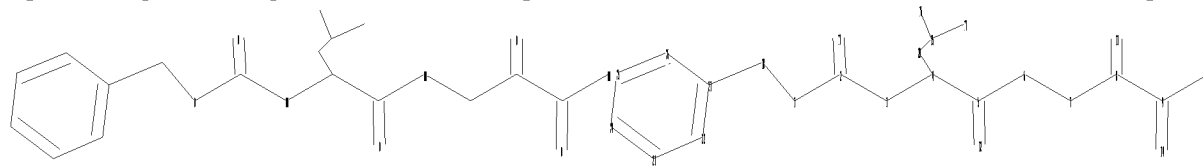
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FILE 'REGISTRY' ENTERED AT 15:58:24 ON 03 DEC 2008

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Uploading C:\Program Files\Stnexp\Queries\10 582015 formula 1 exclude species.str



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1  2  3  4  5  6  7  8  9 10 11 12 13 14 15 16 17 18 20
ring nodes :
21 22 23 24 25 26
chain bonds :
1-2 1-18 2-3 2-11 3-4 4-5 4-20 5-6 5-12 6-7 7-8 8-9 8-13 9-10 9-14
15-17 15-16 15-20 18-21
ring bonds :
21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
1-2 1-18 2-3 2-11 3-4 5-6 5-12 6-7 8-13 9-10 9-14
exact bonds :
4-5 4-20 7-8 8-9 15-17 15-16 15-20 18-21
normalized bonds :
21-22 21-26 22-23 23-24 24-25 25-26
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G1:H,CH3,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,Cy

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Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS
18:CLASS 20:CLASS 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom
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L11 STRUCTURE UPLOADED

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SAMPLE SUBSET SCREEN SEARCH COMPLETED - 14 TO ITERATE
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100.0% PROCESSED 14 ITERATIONS 14 ANSWERS
SEARCH TIME: 00.00.01
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PROJECTIONS (WITHIN SPECIFIED SUBSET): ONLINE **COMPLETE**
PROJECTED ITERATIONS (WITHIN SPECIFIED SUBSET): 56 TO 504
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET): 56 TO 504
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L12 14 SEA SUB=L3 SSS SAM L11

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SEARCH TIME: 00.00.01
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(FILE 'HOME' ENTERED AT 15:40:27 ON 03 DEC 2008)

FILE 'REGISTRY' ENTERED AT 15:40:32 ON 03 DEC 2008

L1 STRUCTURE UPLOADED

L2 14 S L1 SAM

L3 291 S L1 FULL

FILE 'CAPLUS' ENTERED AT 15:40:57 ON 03 DEC 2008

L4 51 S L3

L5 1 S US 20070004643 A1/PN

L6 27 S L4 NOT PATENT/DT

L7 17 S L6 AND PD<20041208

L8 24 S L4 NOT L6

L9 22 S L8 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)

L10 39 S L7 OR L9

FILE 'STNGUIDE' ENTERED AT 15:46:12 ON 03 DEC 2008

FILE 'REGISTRY' ENTERED AT 15:58:24 ON 03 DEC 2008

L11 STRUCTURE UPLOADED

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L13 261 S L11 FULL SUB=L3

=> s l3 not l13

L14 30 L3 NOT L13

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

42.56

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-31.20

FILE 'CAPLUS' ENTERED AT 15:59:10 ON 03 DEC 2008

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FILE COVERS 1907 - 3 Dec 2008 VOL 149 ISS 23

FILE LAST UPDATED: 2 Dec 2008 (20081202/ED)

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http://www.cas.org/legal/infopolicy.html  
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L15 13 L14

=> s l10 and l15

L16 5 L10 AND L15

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L16 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:540563 CAPLUS

DOCUMENT NUMBER: 143:60256

TITLE: Preparation of leucyl  $\alpha$ -ketoamide derivatives as calpain inhibitors

INVENTOR(S): Shirasaki, Yoshihisa; Miyashita, Hiroyuki; Nakamura, Masayuki; Inoue, Jun

PATENT ASSIGNEE(S): Senju Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

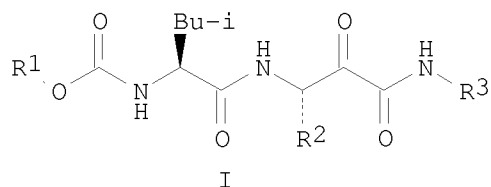
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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WO 2005056519	A1	20050623	WO 2004-JP18692	20041208 <--
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1692098	A1	20060823	EP 2004-807051	20041208 <--
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IN 2006KN01379	A	20070504	IN 2006-KN1379	20060523 <--
US 20070004643	A1	20070104	US 2006-582015	20060607 <--
PRIORITY APPLN. INFO.:			JP 2003-415764	A 20031212 <--
			JP 2004-234164	A 20040811 <--
			WO 2004-JP18692	W 20041208
OTHER SOURCE(S):		CASREACT 143:60256; MARPAT 143:60256		
GI				



AB The invention provides compds. I (R1 is alkyl, alkoxy- or heterocyclylalkyl or heterocyclyl; R2 is alkyl or phenylalkyl; R3 is H, alkyl, halo-, alkoxy- or phenylalkyl or fused polycyclyl), which have potent calpain inhibitory activity, are well absorbed orally and produce good drug levels in blood. Thus, I (R1 = MeOCH<sub>2</sub>CH<sub>2</sub>, R2 = PhCH<sub>2</sub>, R3 = Et) was prepared via peptide coupling reaction and shown to strongly inhibit  $\mu$ -calpain and m-calpain (IC<sub>50</sub> = 0.17 and 0.11 uM, resp.).

IT 854402-43-0P 854402-46-3P 854402-49-6P  
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 854402-53-2P 854402-54-3P 854402-55-4P  
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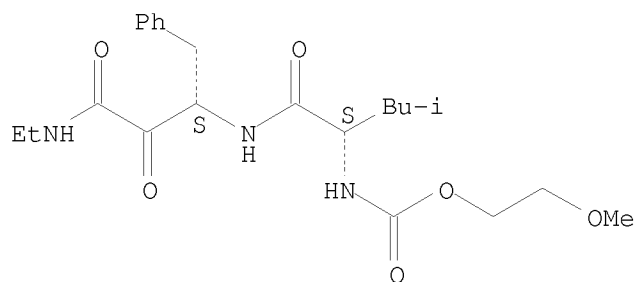
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of leucyl  $\alpha$ -ketoamide derivs. as calpain inhibitors)

RN 854402-43-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

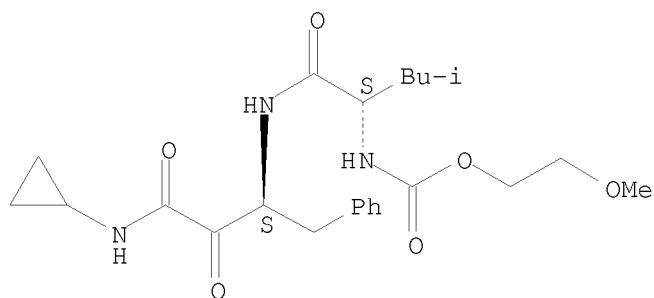
Absolute stereochemistry.



RN 854402-46-3 CAPLUS

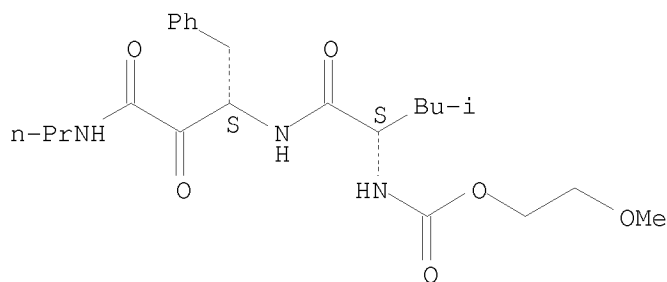
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Absolute stereochemistry. Rotation (+).



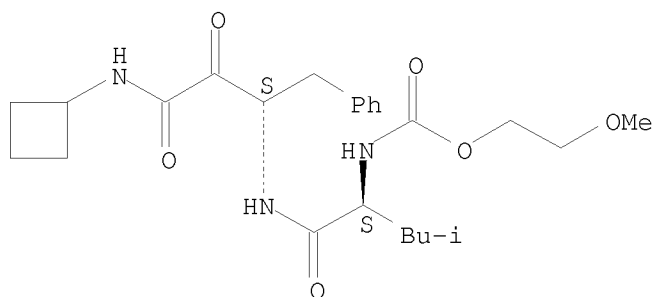
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Absolute stereochemistry.



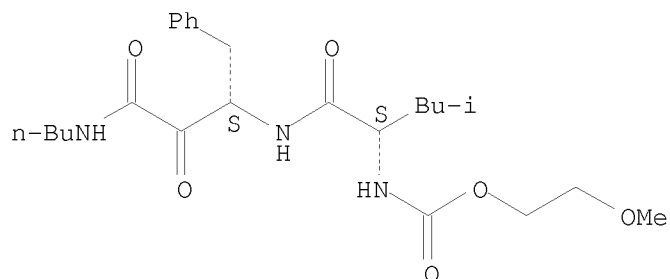
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Absolute stereochemistry.



RN 854402-51-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

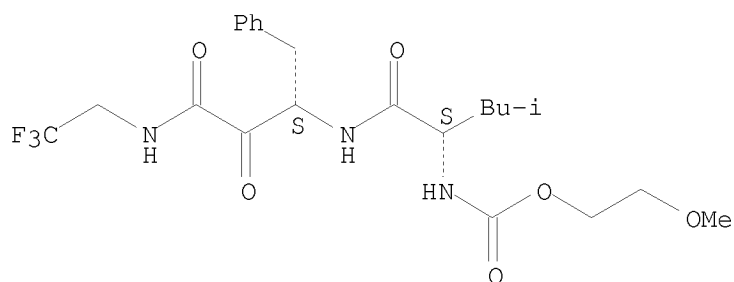
Absolute stereochemistry.



RN 854402-52-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(2,2,2-trifluoroethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

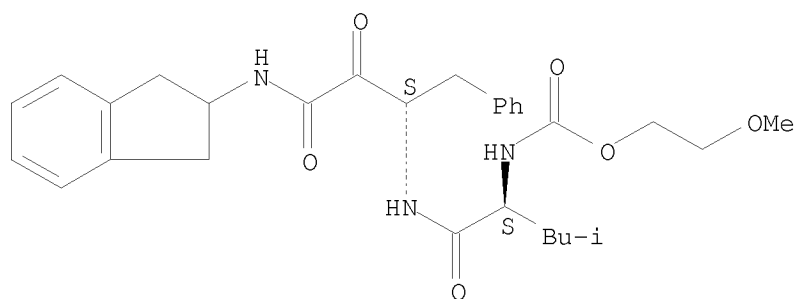
Absolute stereochemistry.



RN 854402-53-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-[(2,3-dihydro-1H-inden-2-yl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

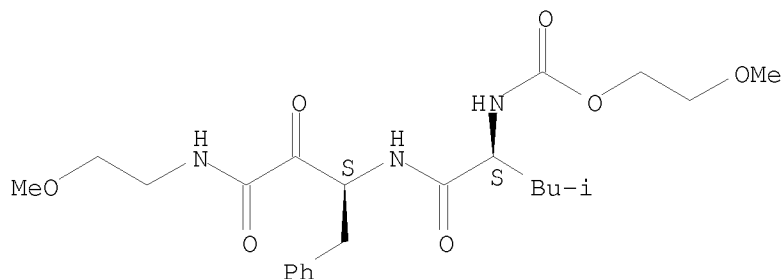
Absolute stereochemistry.



RN 854402-54-3 CAPLUS

CN 12-Oxa-2,5,9-triazatridecanoic acid, 3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, 2-methoxyethyl ester, (3S,6S)- (CA INDEX NAME)

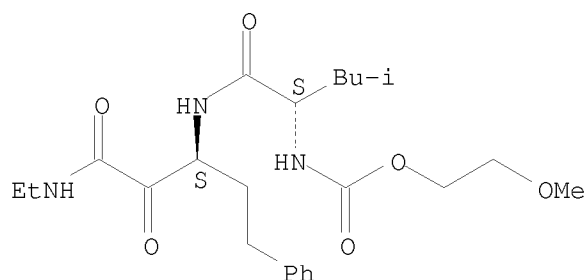
Absolute stereochemistry.



RN 854402-55-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(2-phenylethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

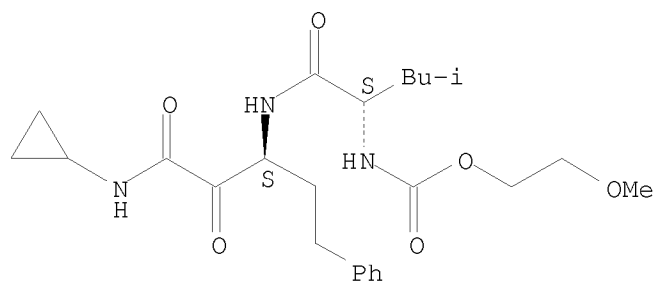
Absolute stereochemistry.



RN 854402-57-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(2-phenylethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

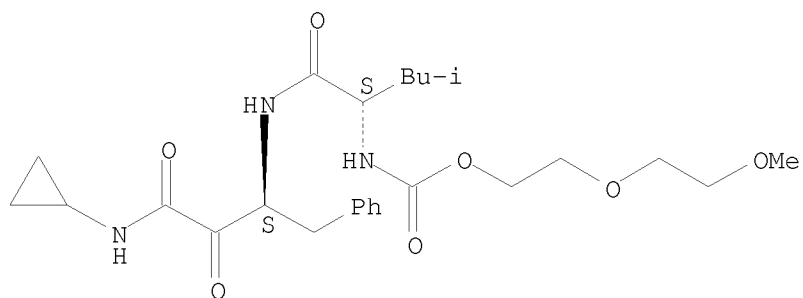
Absolute stereochemistry.



RN 854402-59-8 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-methoxyethoxy)ethyl ester (CA INDEX NAME)

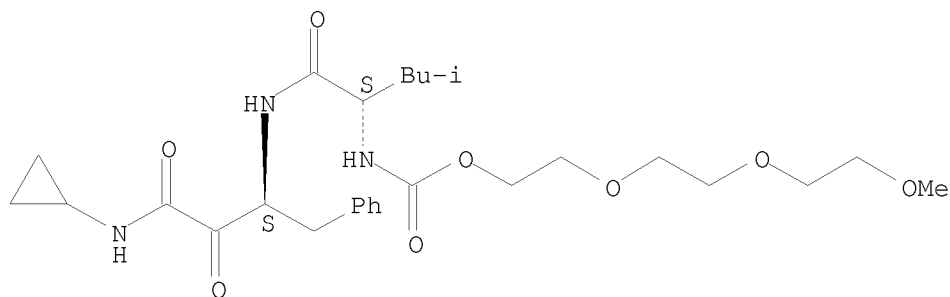
Absolute stereochemistry. Rotation (+).



RN 854402-60-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

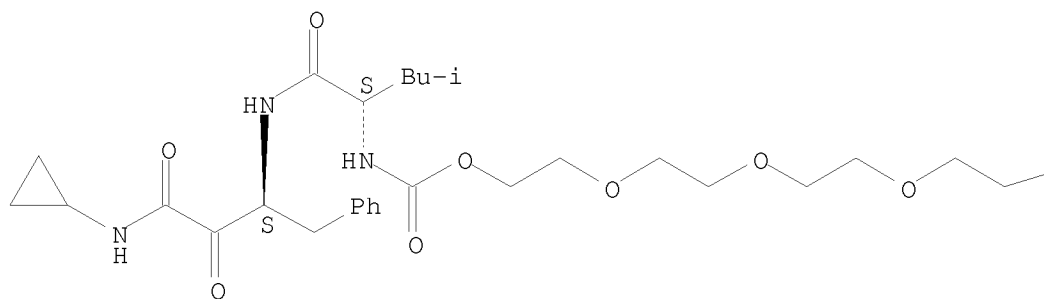


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CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 3,6,9,12-tetraoxatridec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



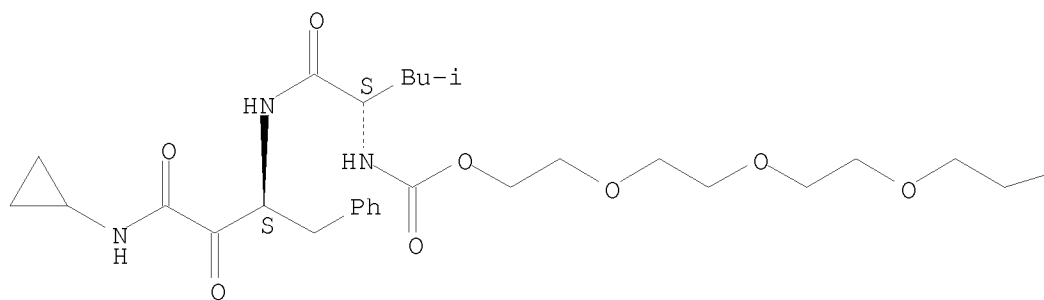


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CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 3,6,9,12,15-pentaoxa-hexadec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

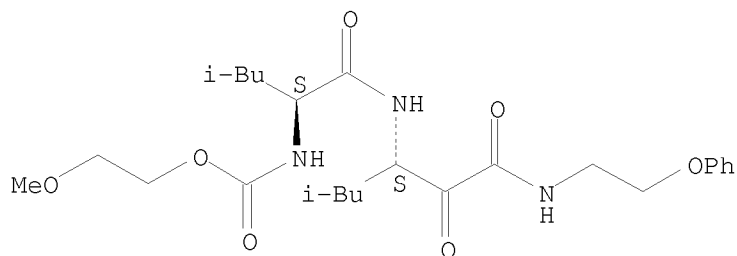


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RN 854402-63-4 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-methyl-1-[oxo[(2-phenoxyethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

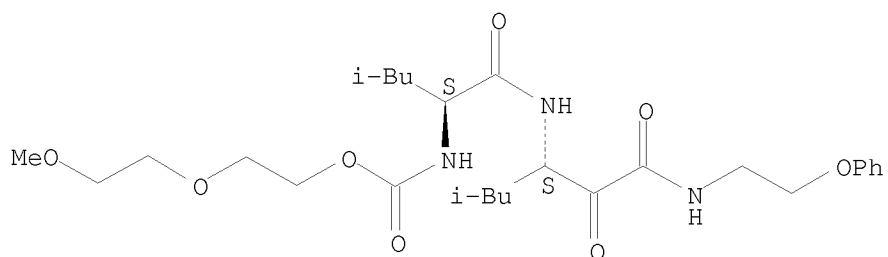


RN 854402-64-5 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-methyl-1-[oxo[(2-

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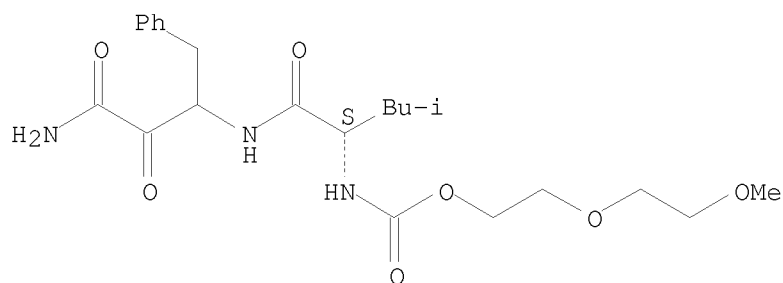
Absolute stereochemistry.



RN 854402-65-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-amino-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-methoxyethoxy)ethyl ester (9CI) (CA INDEX NAME)

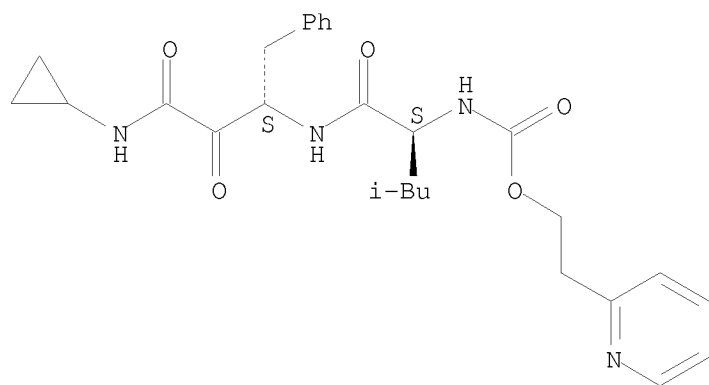
Absolute stereochemistry.



RN 854402-66-7 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-pyridinyl)ethyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

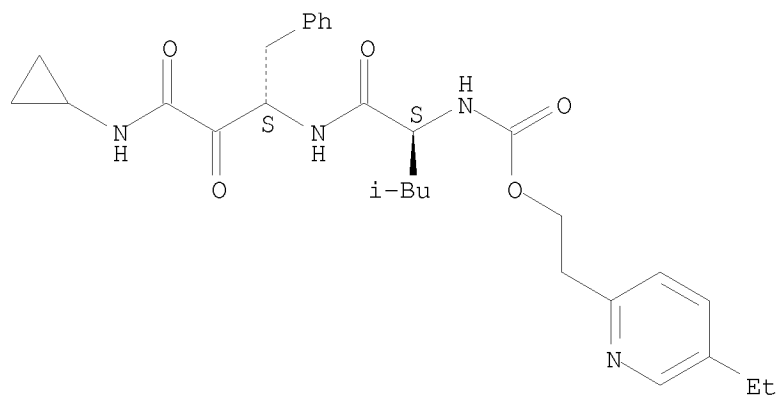


RN 854402-67-8 CAPLUS

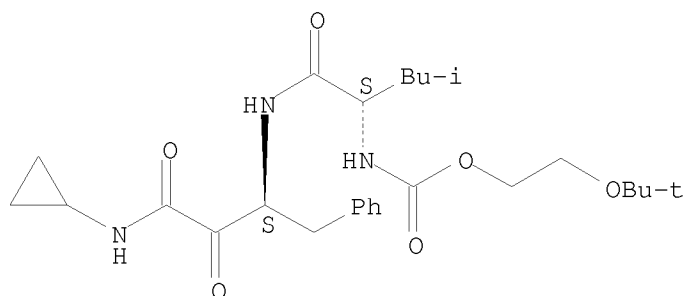
CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(6-methyl-2-pyridinyl)ethyl ester (9CI) (CA INDEX NAME)

CC1=CC=C(C=C1)CSC(=O)NC(=O)SC(=O)NCC2=CC=CC=C2

Absolute stereochemistry. Rotation (-).

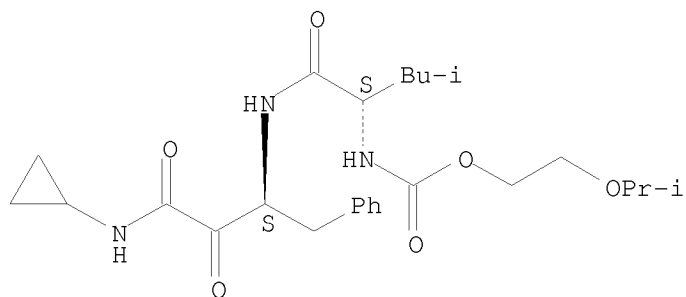


Absolute stereochemistry.



RN 854402-70-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(1-methylethoxy)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:875240 CAPLUS  
 DOCUMENT NUMBER: 139:364944  
 TITLE: Preparation of diketohydrazine derivatives as cysteine protease inhibitors  
 INVENTOR(S): Hatayama, Akira; Tsuruta, Hiroshi; Ochi, Yasuo; Imawaka, Haruo  
 PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 231 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091202	A1	20031106	WO 2003-JP5252	20030424 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
CA 2483998	A1	20031106	CA 2003-2483998 20030424 <--
AU 2003235118	A1	20031110	AU 2003-235118 20030424 <--
EP 1498411	A1	20050119	EP 2003-723188 20030424 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK		
BR 2003009670	A	20050315	BR 2003-9670 20030424 <--
CN 1649831	A	20050803	CN 2003-809191 20030424 <--
NZ 536728	A	20060728	NZ 2003-536728 20030424 <--
JP 3812678	B2	20060823	JP 2004-501947 20030424 <--
MX 2004PA10523	A	20050608	MX 2004-PA10523 20041022 <--
US 20060111303	A1	20060525	US 2004-512348 20041022 <--
KR 838333	B1	20080613	KR 2004-717135 20041025 <--
ZA 2004009502	A	20050815	ZA 2004-9502 20041124 <--
NO 2004005137	A	20041125	NO 2004-5137 20041125 <--
JP 2006199703	A	20060803	JP 2006-46815 20060223 <--
PRIORITY APPLN. INFO.:			JP 2002-123796 A 20020425 <--
			JP 2004-501947 A3 20030424 <--
			WO 2003-JP5252 W 20030424 <--

OTHER SOURCE(S): MARPAT 139:364944

AB Diketohydrazine (3-amino-2-oxopropanoylhydrazine or 3-aminopropionohydrazide) derivs. represented by the following general formula R-AA1-AA2-NR9CR7R8COCONR10NRYRX [wherein R = H, CycA, halo, (un)substituted C1-8 alkyl, R16CO, R16C(S), R16O2C, R16R17NCO, R16SO2, R16COCH2, R16C(S)CH2; CycA = C3-15 mono-, bi-, or tricyclic carbocyclic ring, 3- to 15-membered mono-, bi-, or tricyclic heterocyclic ring containing 1-4 N, 1 or 2 O and/or 1 or 2 S atom(s); R16 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, CycA; R17, R9 = H, C1-4 alkyl, CycA, CycA-C1-4 alkyl; AA1 = a single bond, (un)substituted NR3CR1R2CO, etc.; R1, R2 = H, (un)substituted C1-8 alkyl, CysA, etc.; R3, R7, R8 = H, C1-8 alkyl, CycA, CycA-C1-8 alkyl, etc.; AA2 = a single bond, NR3CR1R2CO, -CycC-CO-, -NR38-CycD-CO-, etc.; CycC = 3- to 17-membered mono or bicyclic heterocyclic ring; CycD = C3-14 mono or bicyclic carbocyclic ring, 3- to 14-membered mono- or bicyclic heterocyclic ring; R38 = group listed in R17; R10, RY, and RX are not defined] and pharmaceutically acceptable salts thereof are prepared. These compds. are inhibitors of cysteine protease, in particular cathepsin K, S, L, B, H, F, Y, or C, calpain, or caspase 1. Because of having a cysteine protease inhibitory activity, they are useful as remedies for inflammatory diseases, immune diseases, ischemic diseases, respiratory diseases, circulatory diseases, blood diseases, nerve diseases, liver/biliary duct diseases, bone/joint diseases, metabolic diseases, or diseases caused by apoptosis or degradation of bioconstituent proteins. The bone/joint diseases include osteoporosis, chronic articular rheumatism, arthritis, osteoarthritis (arthrosis deformans), hypercalcemia, bone metastasis of carcinoma, or bone fracture. Also disclosed is a bone absorption inhibitor containing the above compound. Because of having an elastase inhibitory activity, these compds. are also useful as remedies for COPD (chronic obstructive pulmonary disease) and so on. N'-(3-tert-butyl-1,3-thiazolidin-2-ylidene)-3-cyclohexylcarbonylamino-2-oxo-3-(tetrahydropyran-4-yl)propionohydrazide hydrochloride inhibited cathepsin K with Ki of 2.5 nM. A tablet and an ampule containing N'-(3-methyl-1,3-thiazolidin-2-ylidene)-(3S)-3-cyclohexylcarbonylamino-2-oxo-5-methylhexanohydrazide hydrochloride were described.

IT 620612-98-8P 620613-01-6P 620613-02-7P  
620614-12-2P 620614-16-6P 620614-17-7P  
620614-19-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

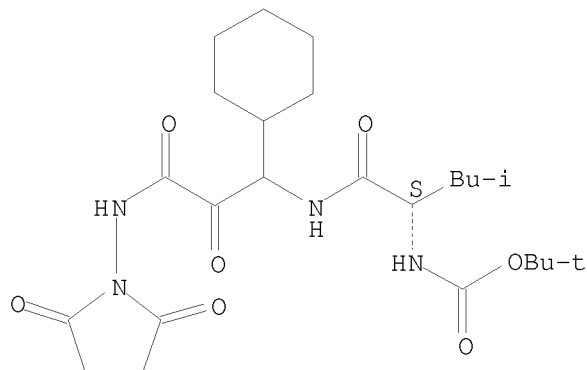
(preparation of diketohydrazine derivs. as cysteine protease inhibitors and

therapeutic agents)

RN 620612-98-8 CAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-3-cyclohexyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo- (9CI) (CA INDEX NAME)

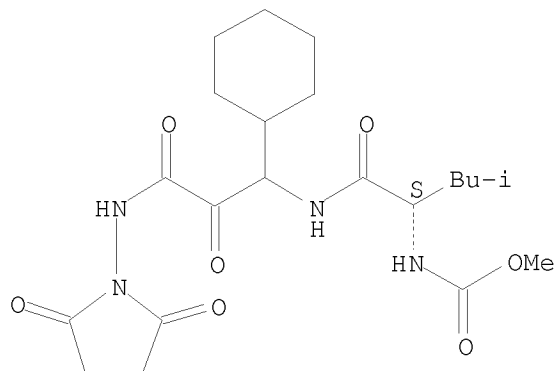
Absolute stereochemistry.



RN 620613-01-6 CAPLUS

CN  $\beta$ -Alaninamide, N-(methoxycarbonyl)-L-leucyl-3-cyclohexyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo- (9CI) (CA INDEX NAME)

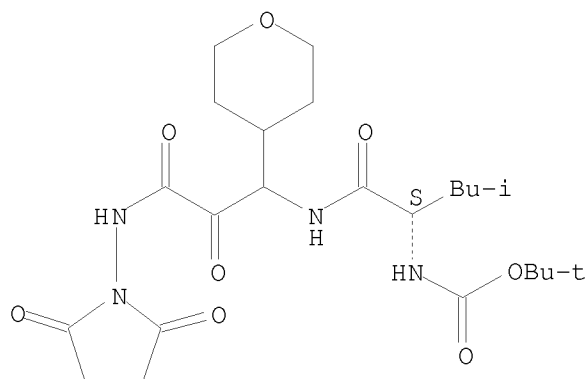
Absolute stereochemistry.



RN 620613-02-7 CAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo-3-(tetrahydro-2H-pyran-4-yl)- (9CI) (CA INDEX NAME)

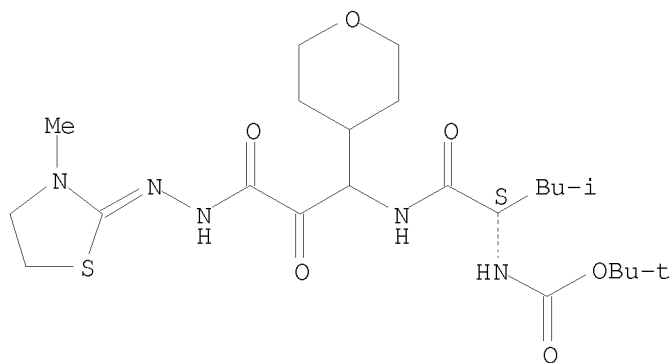
Absolute stereochemistry.



RN 620614-12-2 CAPLUS

CN 2H-Pyran-4-propanoic acid,  $\beta$ -[[[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]tetrahydro- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

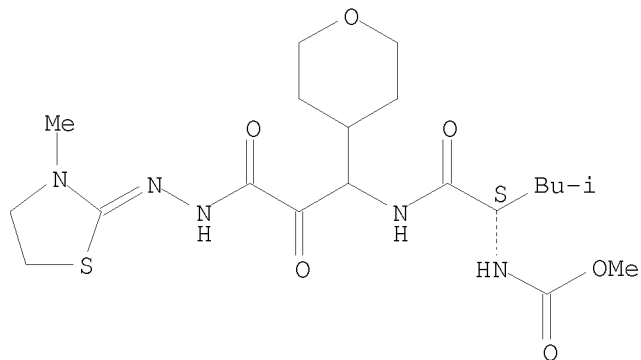
Absolute stereochemistry.  
Double bond geometry unknown.



RN 620614-16-6 CAPLUS

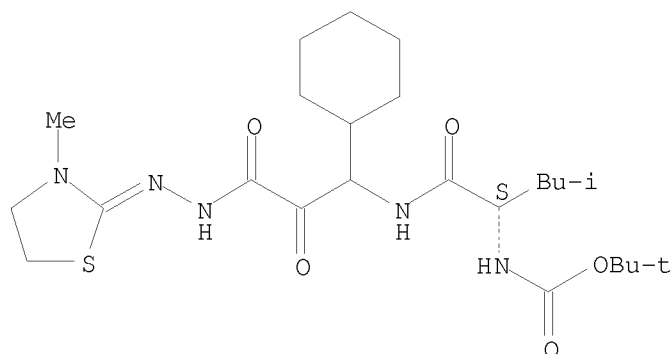
CN 2H-Pyran-4-propanoic acid, tetrahydro- $\beta$ -[[[(2S)-2-[(methoxycarbonyl)amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



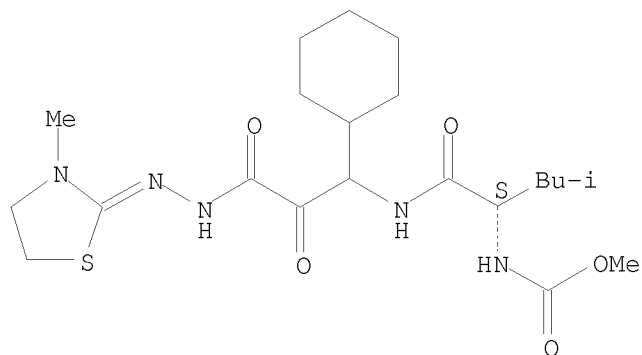
RN 620614-17-7 CAPLUS  
CN Cyclohexanepropanoic acid,  $\beta$ -[[[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



RN 620614-19-9 CAPLUS  
CN Cyclohexanepropanoic acid,  $\beta$ -[[[(2S)-2-[(methoxycarbonyl)amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1995:731521 CAPLUS  
DOCUMENT NUMBER: 123:144653  
ORIGINAL REFERENCE NO.: 123:25801a,25804a  
TITLE: Preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors.  
INVENTOR(S): Harbeson, Scott L.; Straub, Julie Ann  
PATENT ASSIGNEE(S): Alkermes, Inc., USA  
SOURCE: PCT Int. Appl., 80 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1



## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500535	A1	19950105	WO 1994-US6497	19940609 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5541290	A	19960730	US 1993-82274	19930624 <--
AU 9472452	A	19950117	AU 1994-72452	19940609 <--
PRIORITY APPLN. INFO.:			US 1993-82274	A 19930624 <--
			WO 1994-US6497	W 19940609 <--

OTHER SOURCE(S): CASREACT 123:144653; MARPAT 123:144653

AB M(A1)xA2NHCHR1COCONHR2SO2R3 (sic), M(A1)xA2NHCHR1COCONHR5R6, etc.; [M = H, H2NCO, H2NCS, H2NSO2, R7CS, R7NHCS, R7CO, R7SO2, R7O2C, etc.; R7 = 1-adamantyl, (substituted) alkyl, alkyl, Ph, naphthyl, phenylalkyl, phenoxyalkyl, etc.; A1 = D-, L-, or nonchiral amino acid, e.g., Ala, Val, Leu, Ile, Met, Tyr, Asn, Gln,  $\beta$ -Ala, Sar, Orn, O-ethylserine, pipecolic acid, cyclohexylalanine, pyridylalanine, p-nitrophenylalanine,  $\alpha$ -aminoheptanoic acid, citrulline, 2-azetidinecarboxylic acid, trifluoroleucine, etc.; x = 0-3; A2 = D- or L-amino acid capable of imparting calpain specificity; R1 = alkyl, cycloalkyl, fluoroalkyl; R2 = alkyl, cycloalkyl, phenylalkyl, (substituted) phenylalkyl, phenylcycloalkyl; R3 = R2, OH, OR2, NH2, NHR2; NR2R2; R5, R6 = H, alkyl, cycloalkyl, (substituted) phenylalkyl, phenylcycloalkyl, morpholinoalkyl, piperidinoalkyl, etc.], were prepared Thus, Z-Leu-Abu-CONHET (Abu = L- $\alpha$ -aminobutyric acid) (solution phase preparation given) inhibited calpain I with Ki = 77 nM.

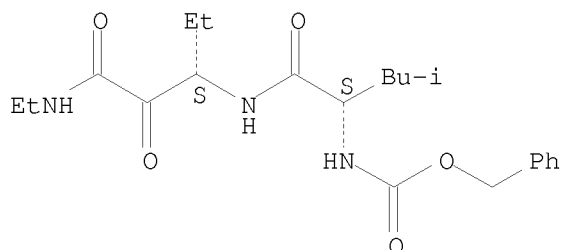
IT 144231-76-5P 144248-93-1P 153371-08-5P  
 160801-90-1P 160801-91-2P 160801-92-3P  
 161021-87-0P 166195-97-7P 166195-98-8P  
 166195-99-9P 166196-00-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors)

RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

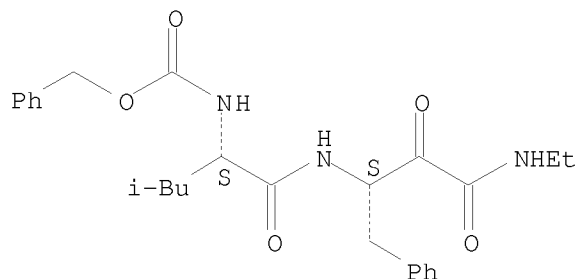
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

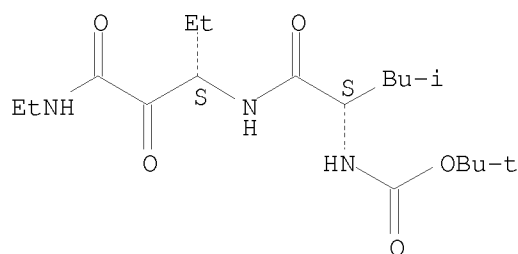
Absolute stereochemistry.



RN 153371-08-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

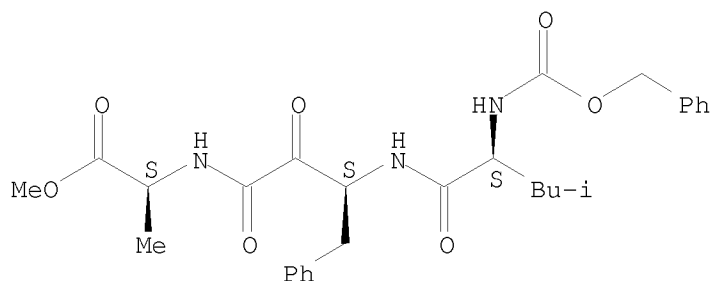
Absolute stereochemistry.



RN 160801-90-1 CAPLUS

CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-, methyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

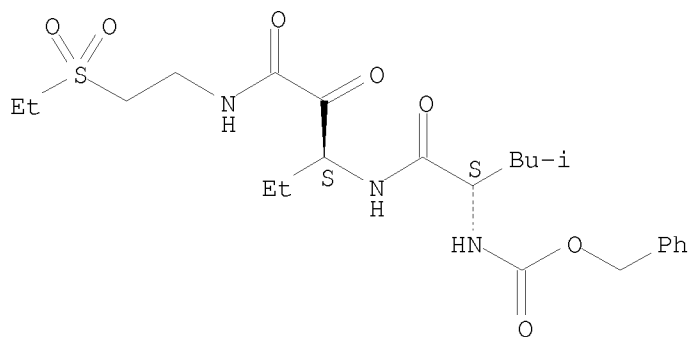
Absolute stereochemistry.



RN 160801-91-2 CAPLUS

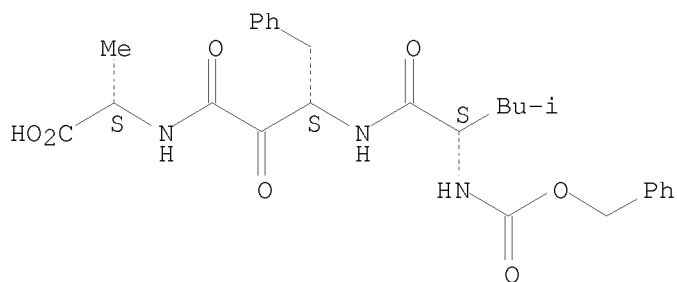
CN 12-Thia-2,5,9-triazatetradecanoic acid, 6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, 12,12-dioxide, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



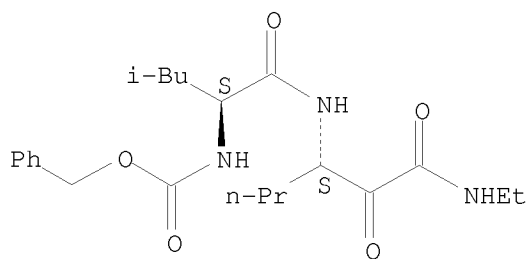
RN 160801-92-3 CAPLUS  
 CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-  
 [[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-,  
 [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

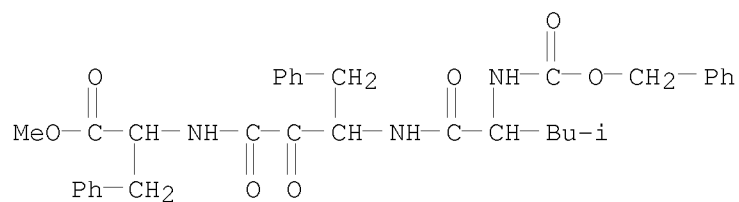


RN 161021-87-0 CAPLUS  
 CN Carbamic acid, [1-[[[1-[(ethylamino)oxoacetyl]butyl]amino]carbonyl]-3-  
 methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

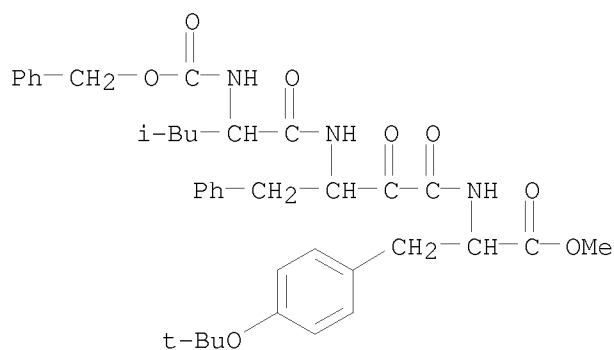


RN 166195-97-7 CAPLUS  
 CN L-Phenylalanine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-  
 aminobutanoyl-, methyl ester (9CI) (CA INDEX NAME)



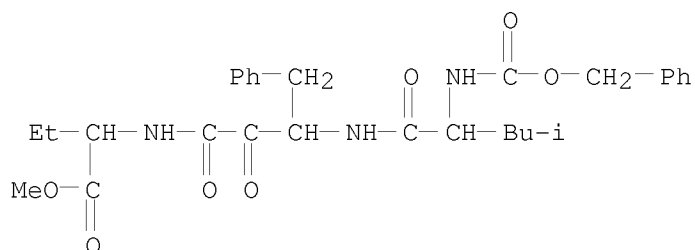
RN 166195-98-8 CAPLUS

CN L-Tyrosine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-O-(1,1-dimethylethyl)-, methyl ester (9CI) (CA INDEX NAME)



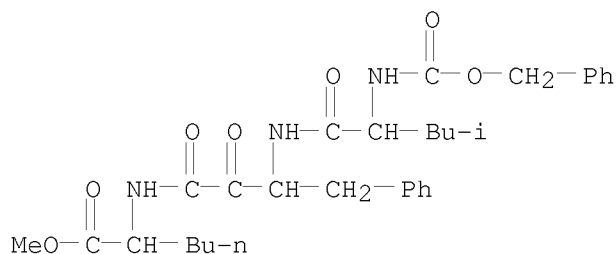
RN 166195-99-9 CAPLUS

CN Butanoic acid, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-L-2-amino-, methyl ester (9CI) (CA INDEX NAME)



RN 166196-00-5 CAPLUS

CN L-Norleucine, N-[(phenylmethoxy)carbonyl]-L-leucyl-2-oxo-4-phenyl-(S)-3-aminobutanoyl-, methyl ester (9CI) (CA INDEX NAME)

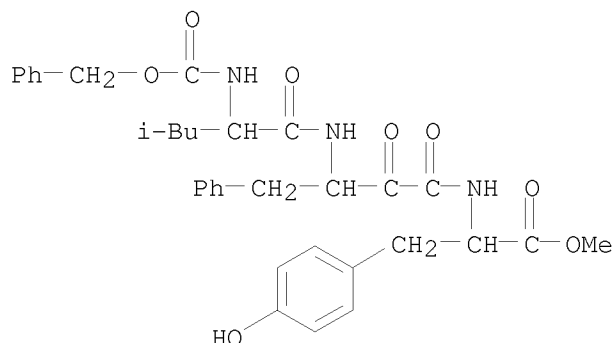


IT 848487-37-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors)

RN 848487-37-6 CAPLUS

CN 2-Oxa-4,7,11-triazatridecan-13-oic acid,  
12-[(4-hydroxyphenyl)methyl]-5-(2-methylpropyl)-3,6,9,10-tetraoxo-1-phenyl-  
8-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



L16 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:31017 CAPLUS

DOCUMENT NUMBER: 122:133766

ORIGINAL REFERENCE NO.: 122:24963a,24966a

TITLE: Stereospecific Synthesis of Peptidyl  $\alpha$ -Keto  
Amides as Inhibitors of Calpain

AUTHOR(S): Harbeson, Scott L.; Abelleira, Susan M.; Akiyama,  
Alan; Barrett, Robert, III; Carroll, Renee M.; Straub,  
Julie Ann; Tkacz, Jaroslaw N.; Wu, Chichih; Musso,  
Gary F.

CORPORATE SOURCE: Alkermes Inc., Cambridge, MD, 02139-4136, USA

SOURCE: Journal of Medicinal Chemistry (1994),  
37(18), 2918-29

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peptidyl  $\alpha$ -keto amides have been synthesized and tested as inhibitors of the cysteine protease calpain. A stereospecific synthesis was devised in which protected dipeptidyl  $\alpha$ -hydroxy amides were oxidized with TEMPO/hypochlorite to the corresponding  $\alpha$ -keto amides. This oxidation was accomplished in good yields and without epimerization of the chiral center adjacent to the ketone. The potent inhibition of porcine calpain I by the L,L diastereomers, combined with the poor inhibition by the L,D diastereomers, established the requirement for the all-L stereochem. of the active inhibitor. The early lead inhibitors were very hydrophobic and, therefore, poorly soluble in aqueous solns. Using the stereospecific route, new compds. were prepared with polar groups at the C- and N-termini. These modifications resulted in more soluble inhibitors that were still potent inhibitors of calpain. Studies of the stability of these  $\alpha$ -keto amides showed that absolute stereochem. can be maintained in acidic and unbuffered environments but general base-catalyzed epimerization of the chiral center adjacent to the ketone occurred rapidly. The  $\alpha$ -hydroxy precursors were inactive as inhibitors of calpain, which supports the hypothesis that the  $\alpha$ -keto compds. reversibly form an enzyme-bound tetrahedral species that results from the nucleophilic addition of the catalytic thiol of calpain to the electrophilic ketone of the inhibitor.

IT 144231-76-5P 144248-93-1P 153371-08-5P

160801-71-8P 160801-90-1P 160801-91-2P

160801-92-3P 160868-23-5P 161021-87-0P

161021-88-1P

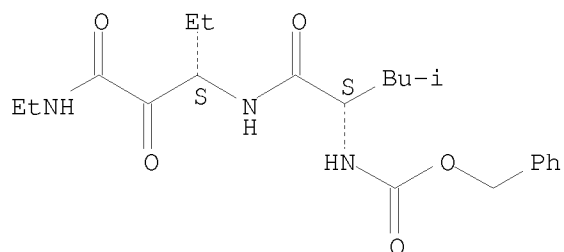
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(stereospecific synthesis of peptidyl  $\alpha$ -keto amides as inhibitors of calpain)

RN 144231-76-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

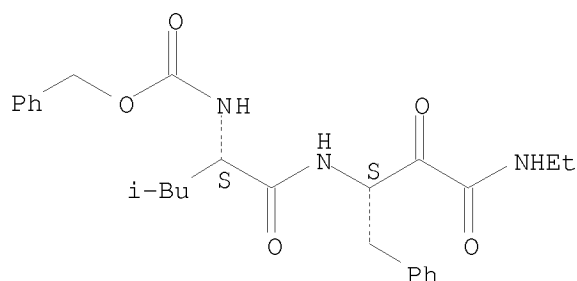
Absolute stereochemistry.



RN 144248-93-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

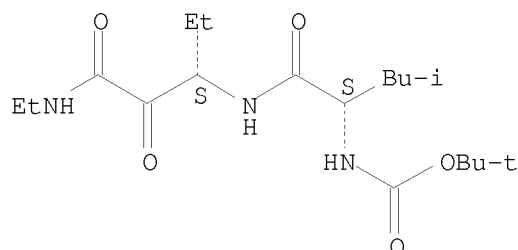
Absolute stereochemistry.



RN 153371-08-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

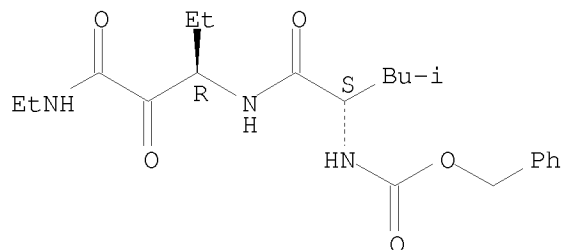
Absolute stereochemistry.



RN 160801-71-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

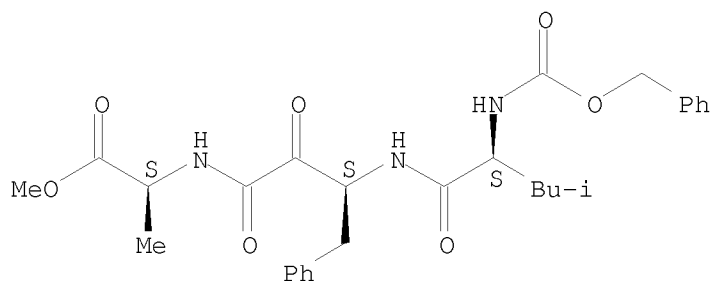
Absolute stereochemistry.



RN 160801-90-1 CAPLUS

CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-[[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-, methyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

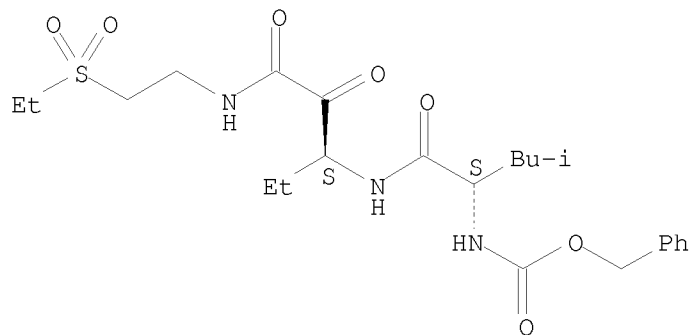
Absolute stereochemistry.



RN 160801-91-2 CAPLUS

CN 12-Thia-2,5,9-triazatetradecanoic acid, 6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, 12,12-dioxide, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

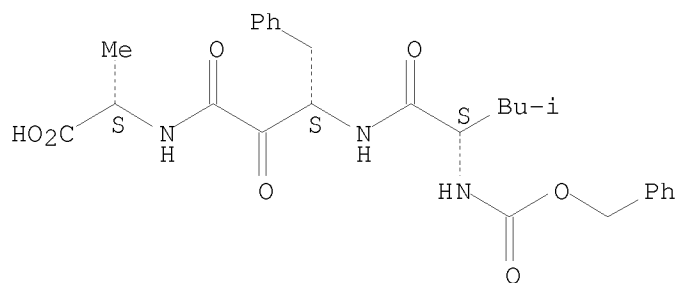
Absolute stereochemistry.



RN 160801-92-3 CAPLUS

CN L-Alanine, N-[3-[[4-methyl-1-oxo-2-[[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1,2-dioxo-4-phenylbutyl]-, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

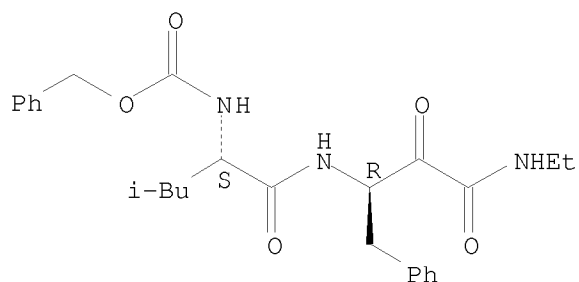
Absolute stereochemistry.



RN 160868-23-5 CAPLUS

CN Carbamic acid, [1-[[[3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

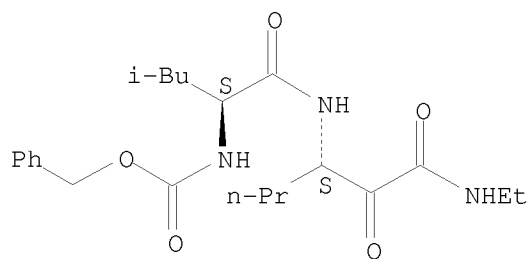
Absolute stereochemistry.



RN 161021-87-0 CAPLUS

CN Carbamic acid, [1-[[[1-[(ethylamino)oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

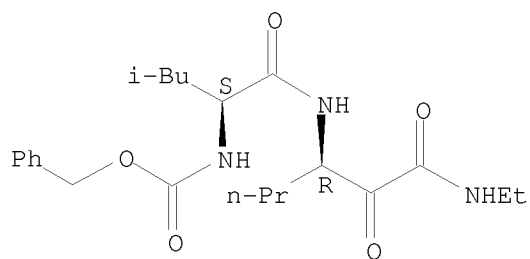


RN 161021-88-1 CAPLUS

CN Carbamic acid, [1-[[[1-[(ethylamino)oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L16 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:153723 CAPLUS

DOCUMENT NUMBER: 120:153723

ORIGINAL REFERENCE NO.: 120:26825a,26828a

TITLE: Use of calpain inhibitors in the inhibition and treatment of medical conditions associated with increased calpain activity

INVENTOR(S): Eveleth, David D., Jr.; Lynch, Gary; Powers, James C.; Bartus, Raymond T.

PATENT ASSIGNEE(S): Cortex Pharmaceuticals, Inc., USA; Georgia Tech Research Corp.

SOURCE: PCT Int. Appl., 255 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9400095	A2	19940106	WO 1993-US6143	19930624 <--
WO 9400095	A3	19940317		
W:	AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9345449	A	19940124	AU 1993-45449	19930624 <--
JP 09500087	T	19970107	JP 1993-502621	19930624 <--
PRIORITY APPLN. INFO.:			US 1992-903800	A2 19920624 <--
			US 1993-34996	A2 19930316 <--
			US 1993-72609	A2 19930601 <--
			WO 1993-US6143	A 19930624 <--

AB Medical conditions in mammals (e.g. cardiac muscle tissue damage, cataracts, smooth muscle damage, and vasospasm) associated with increased proteolytic activity of calpain are treated by administering a pharmaceutical composition containing a calpain inhibitor in a pharmacol. effective

amount The inhibitor is a peptide keto compound, substituted heterocyclic compound, or halo ketone peptide. Also, a method of inhibiting proliferation of smooth muscle cells and thereby preventing the restenosis of a blood vessel which has undergone therapeutic angioplasty includes the administration of a calpain inhibitor to the blood vessel during or after the angioplasty. Further, methods of blocking the establishment of the tonically contracted state in smooth muscle and relaxing tonically contracted smooth muscle are disclosed. These methods involve the administration of a calpain inhibitor, thereby reducing or preventing smooth muscle contraction associated with vasospasm and bronchospasm.

IT 144231-72-1 144231-73-2 144231-74-3

144231-75-4 144231-76-5 144231-77-6  
 144231-78-7 144231-79-8 144231-80-1  
 144231-81-2 144231-82-3 144231-83-4  
 144231-84-5 144231-85-6 144248-93-1  
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 144863-87-6 153370-23-1 153370-24-2  
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 153370-71-9 153370-72-0 153370-73-1  
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 153370-92-4 153371-08-5

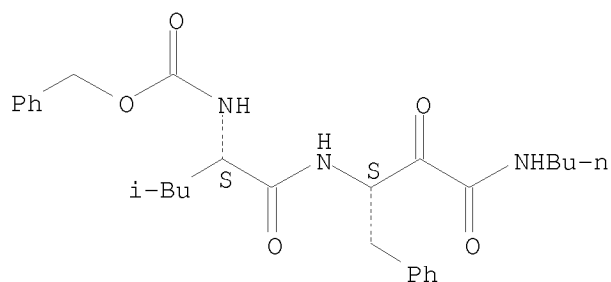
RL: BIOL (Biological study)

(as calpain inhibitor, heart and vascular disease treatment with)

RN 144231-72-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

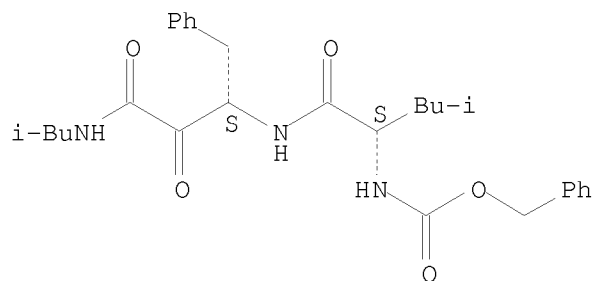
Absolute stereochemistry.



RN 144231-73-2 CAPLUS

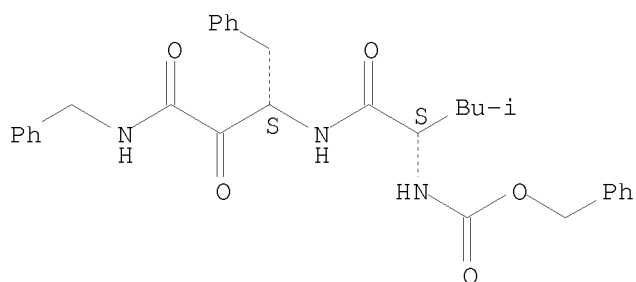
CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-[(2-methylpropyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



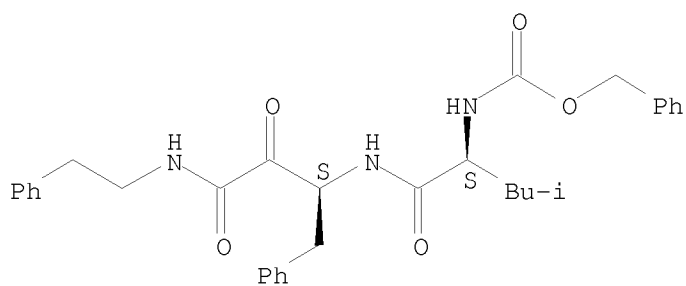
RN 144231-74-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



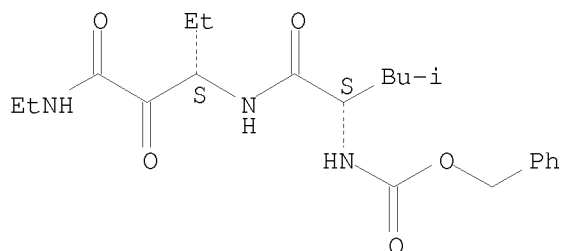
RN 144231-75-4 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-3-[(2-phenylethyl)amino]-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



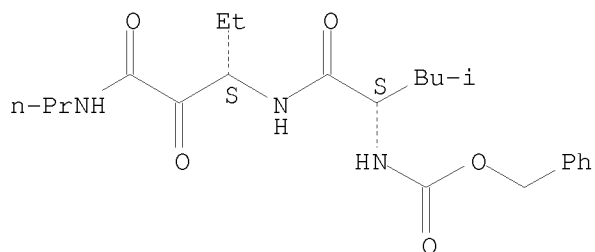
RN 144231-76-5 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



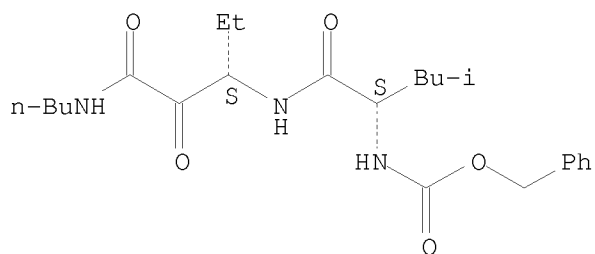
RN 144231-77-6 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



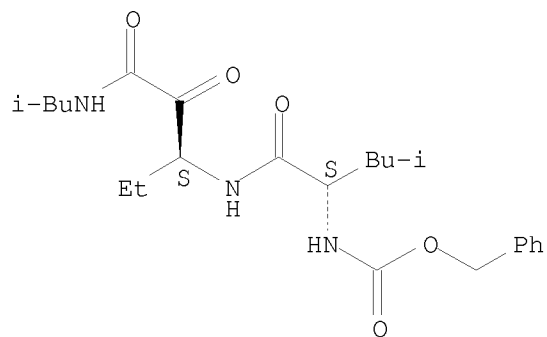
RN 144231-78-7 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



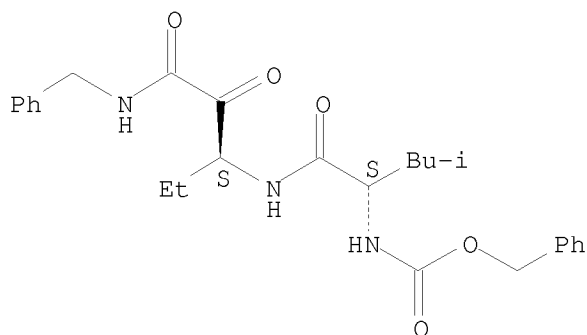
RN 144231-79-8 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-methylpropyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



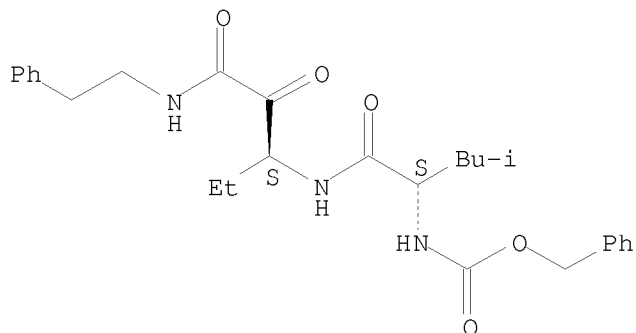
RN 144231-80-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(phenylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



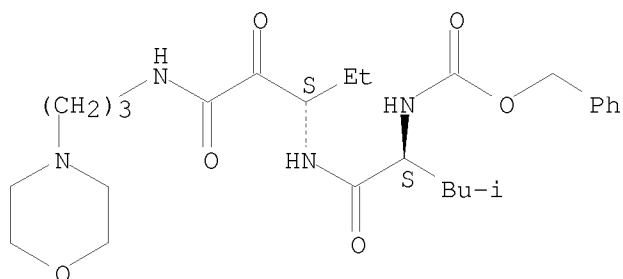
RN 144231-81-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(2-phenylethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144231-82-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

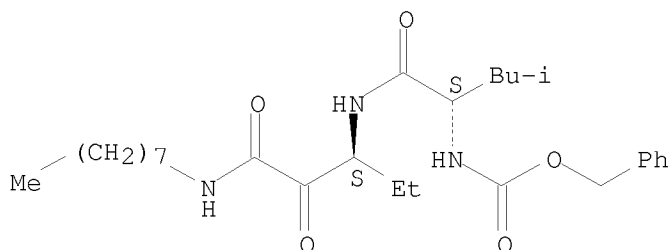
Absolute stereochemistry.



RN 144231-83-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

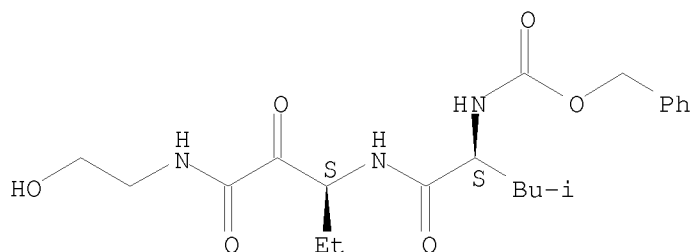
Absolute stereochemistry.



RN 144231-84-5 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-[(2-hydroxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

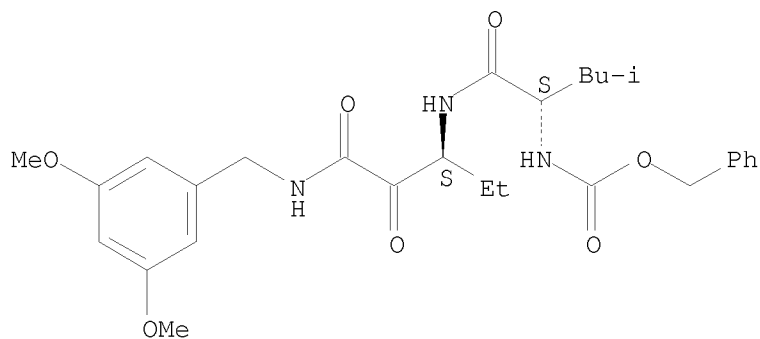
Absolute stereochemistry.



RN 144231-85-6 CAPLUS

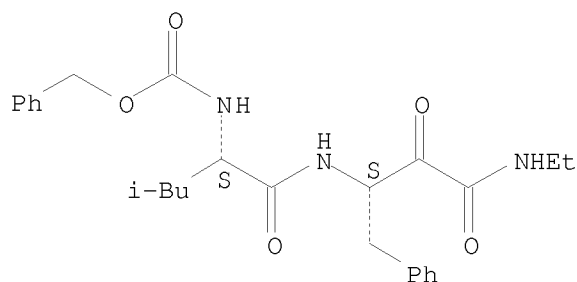
CN Carbamic acid, [(1S)-1-[[[(1S)-3-[[[(3,5-dimethoxyphenyl)methyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



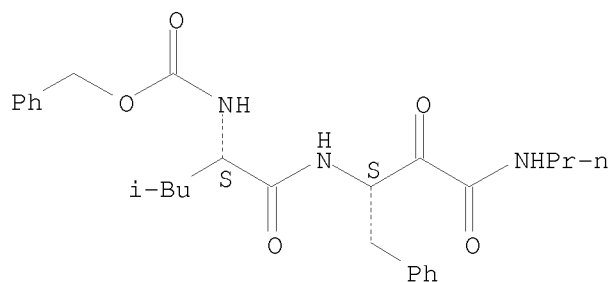
RN 144248-93-1 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



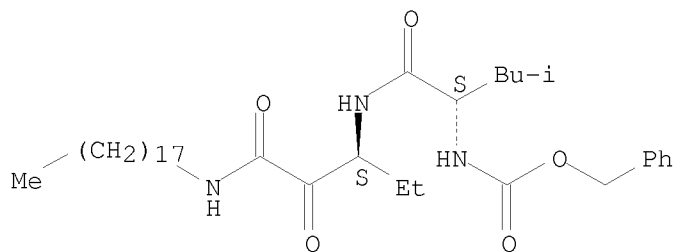
RN 144248-94-2 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144248-95-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-3-(octadecylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

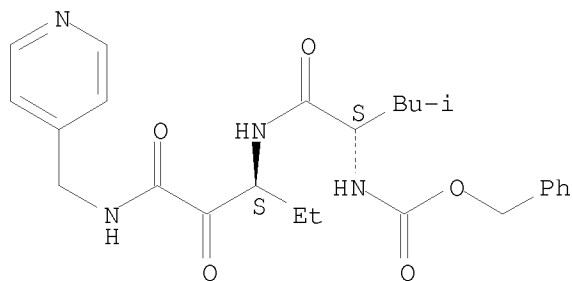
Absolute stereochemistry.



RN 144248-96-4 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-1-ethyl-2,3-dioxo-3-[(4-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

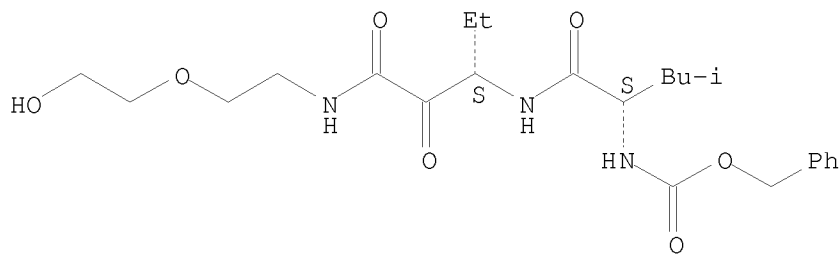
Absolute stereochemistry.



RN 144863-87-6 CAPLUS

CN 12-Oxa-2,5,9-triazatetradecanoic acid, 6-ethyl-14-hydroxy-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, (3S,6S)- (CA INDEX NAME)

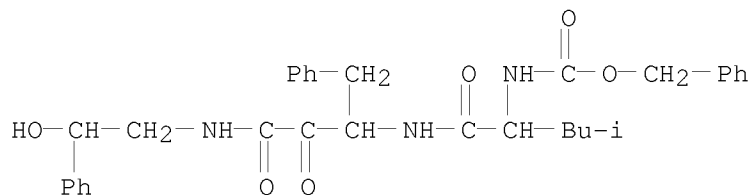
Absolute stereochemistry.



RN 153370-23-1 CAPLUS

CN Carbamic acid, [1-[[[3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

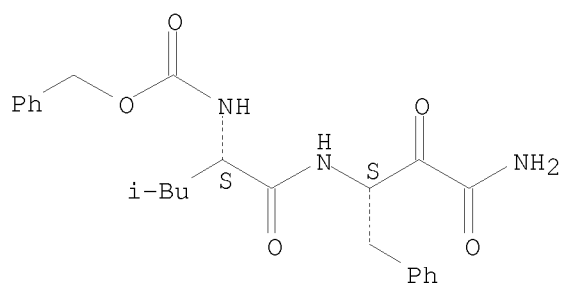




RN 153370-24-2 CAPLUS

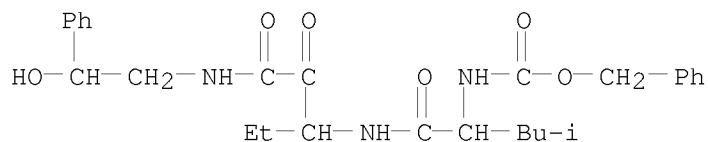
CN Carbamic acid, [1-[[[3-amino-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-25-3 CAPLUS

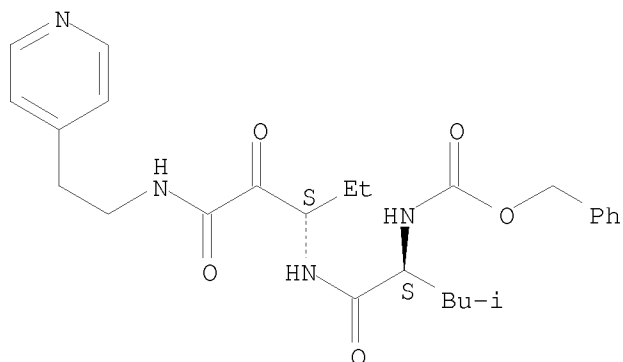
CN Carbamic acid, [1-[[[1-ethyl-3-[(2-hydroxy-2-phenylethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-33-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2-(4-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

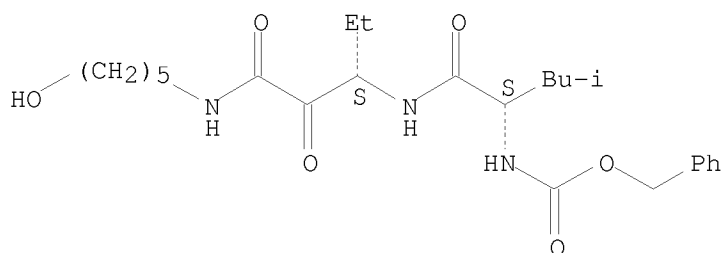
Absolute stereochemistry.



RN 153370-34-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(5-hydroxypentyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

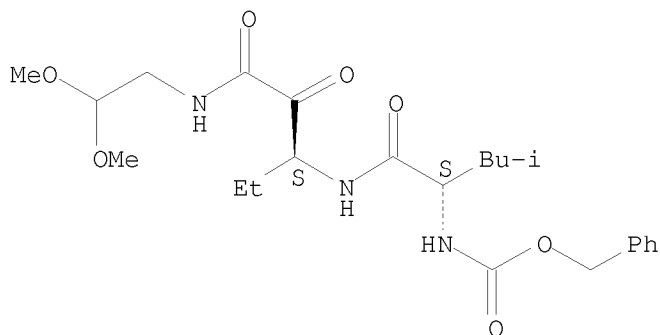
Absolute stereochemistry.



RN 153370-35-5 CAPLUS

CN 2-Oxa-5,9,12-triazatridecan-13-oic acid, 8-ethyl-3-methoxy-11-(2-methylpropyl)-6,7,10-trioxo-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

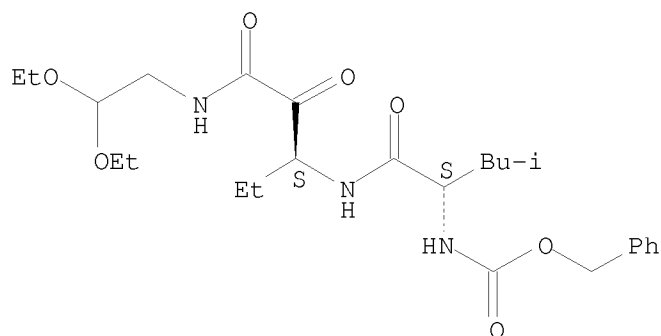
Absolute stereochemistry.



RN 153370-36-6 CAPLUS

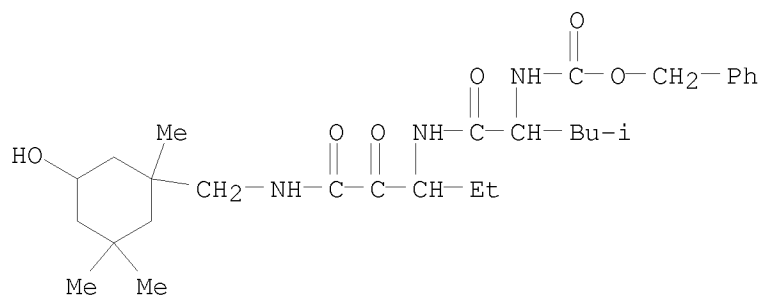
CN 12-Oxa-2,5,9-triazatetradecanoic acid, 11-ethoxy-6-ethyl-3-(2-methylpropyl)-4,7,8-trioxo-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-37-7 CAPLUS

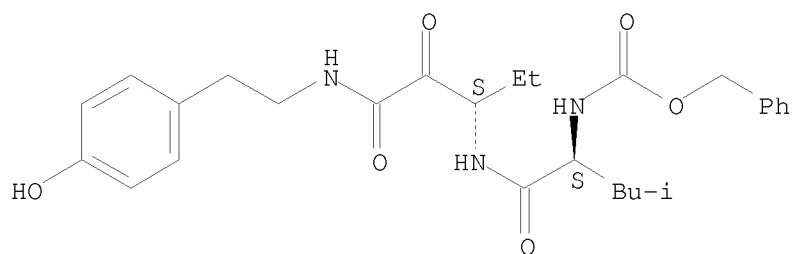
CN Carbamic acid, [1-[[[1-ethyl-3-[[5-(2-ethoxy-1-ethoxyethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-38-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-hydroxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

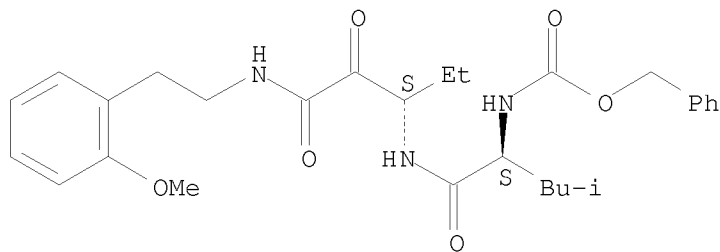
Absolute stereochemistry.



RN 153370-39-9 CAPLUS

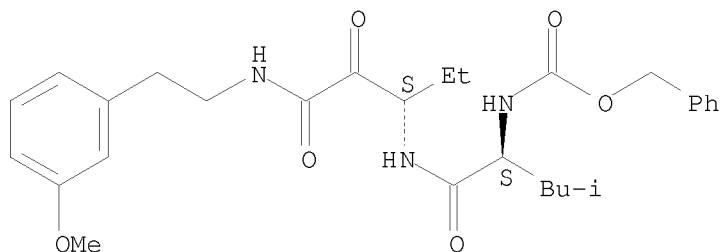
CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(2-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



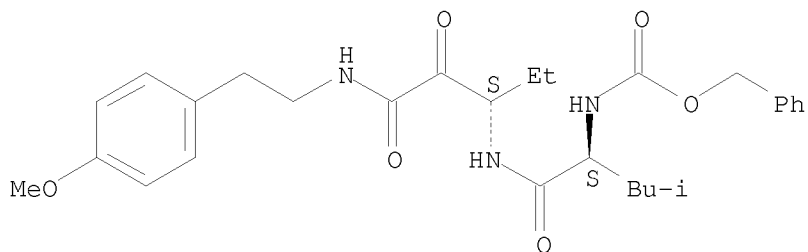
RN 153370-40-2 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(3-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



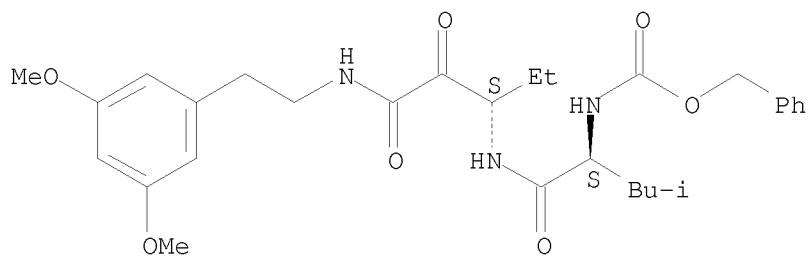
RN 153370-41-3 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



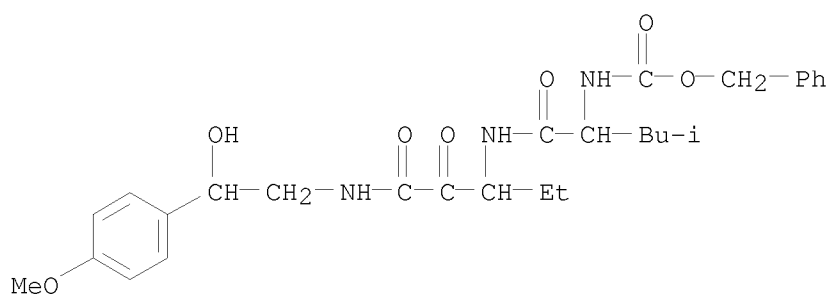
RN 153370-42-4 CAPLUS  
 CN Carbamic acid, [1-[[[3-[[2-(3,5-dimethoxyphenyl)ethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



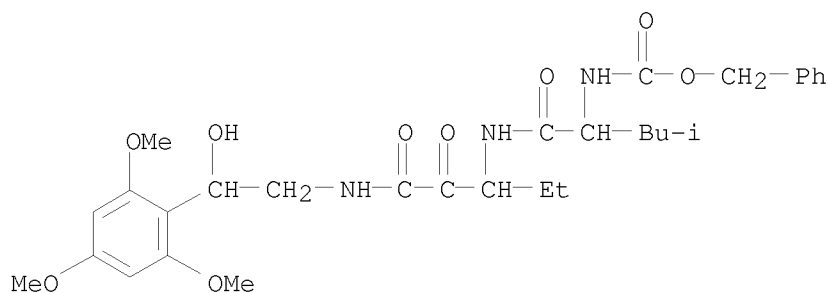
RN 153370-43-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-methoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



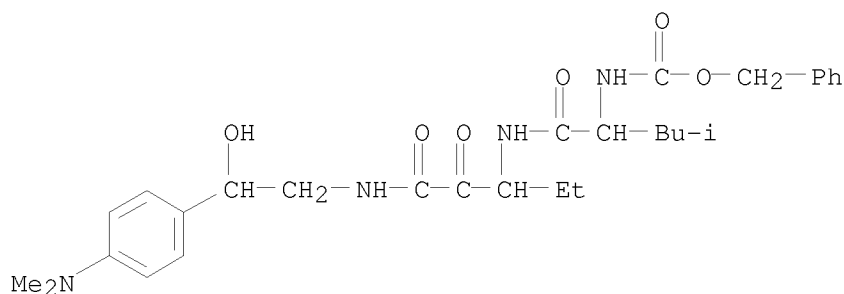
RN 153370-44-6 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(2,4,6-trimethoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



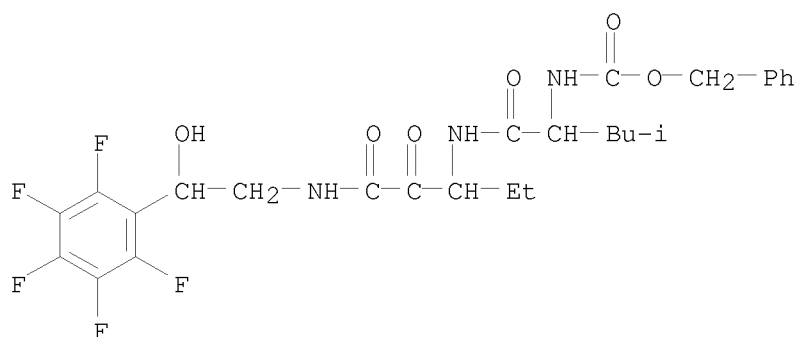
RN 153370-45-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



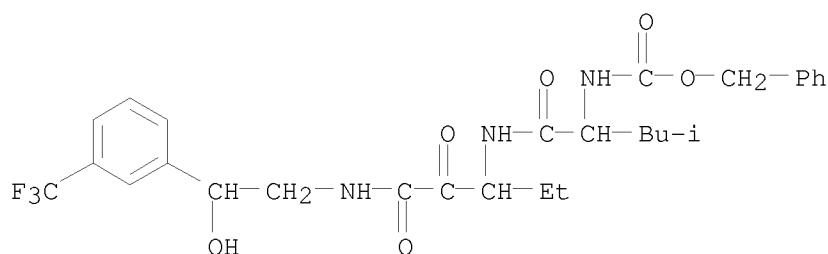
RN 153370-46-8 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



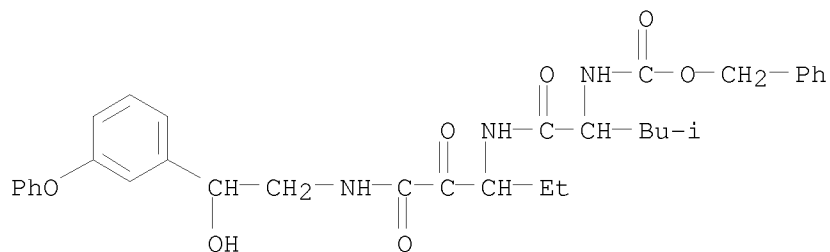
RN 153370-47-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



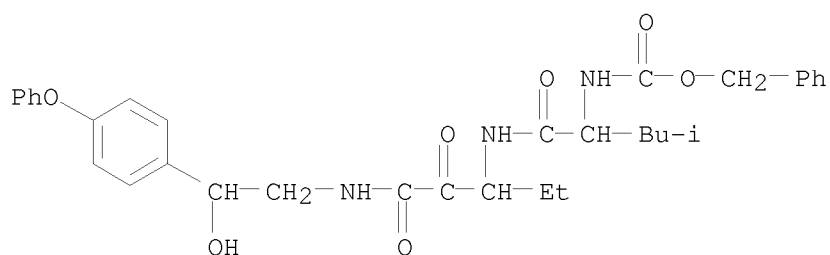
RN 153370-48-0 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



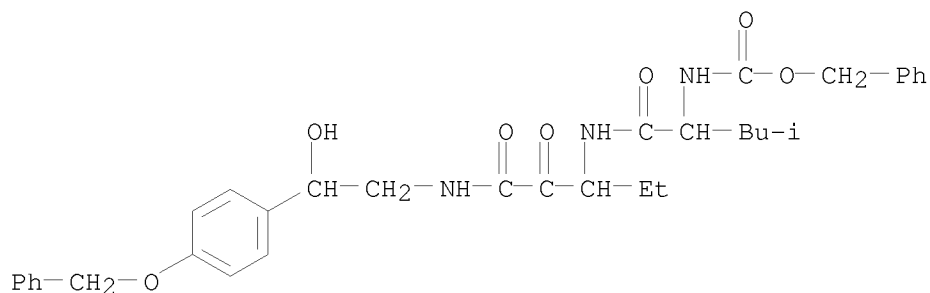
RN 153370-49-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



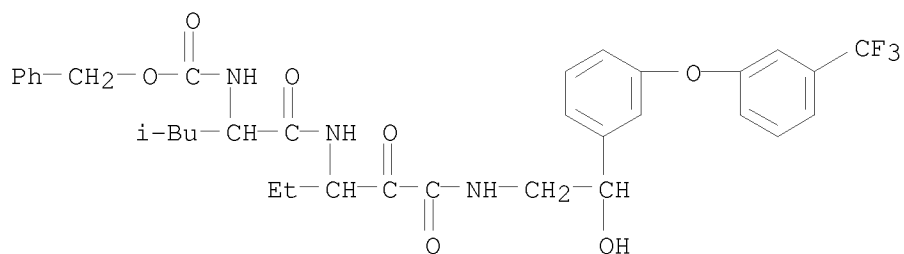
RN 153370-50-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



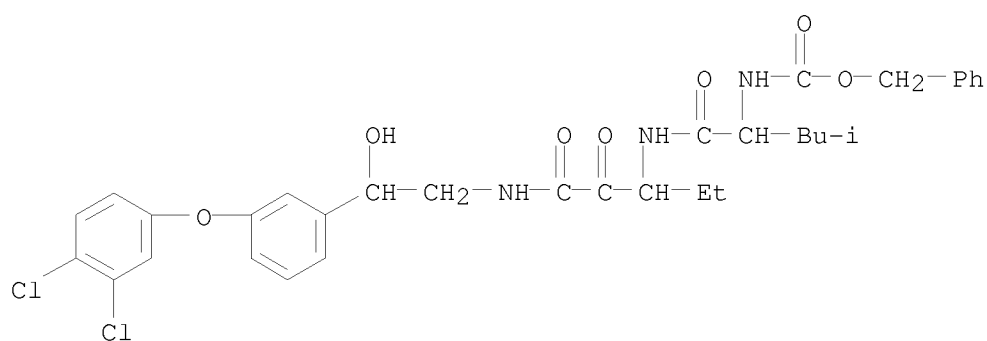
RN 153370-51-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



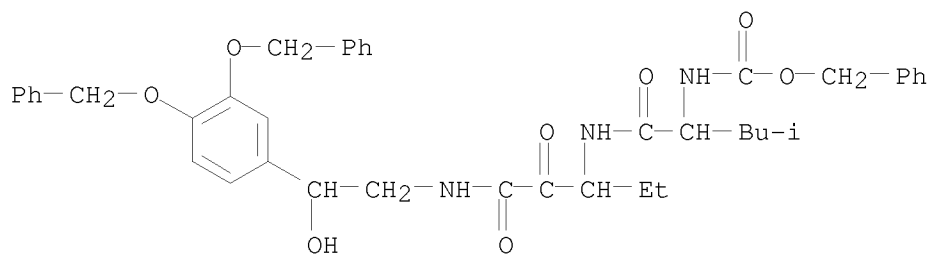
RN 153370-52-6 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-53-7 CAPLUS

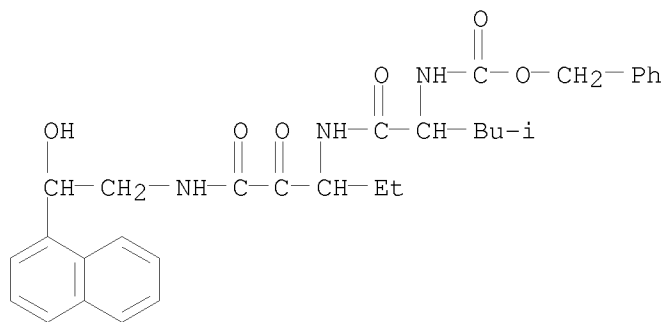
CN Carbamic acid, [1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-54-8 CAPLUS

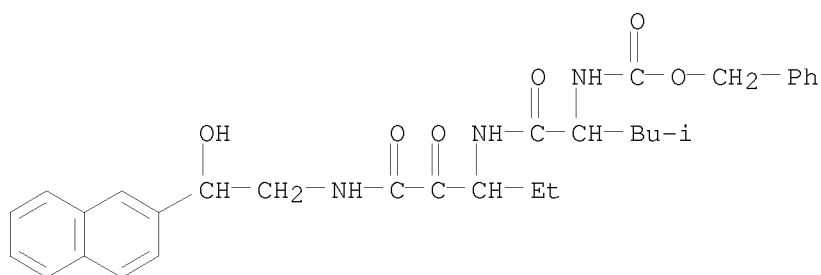
CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(1-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)





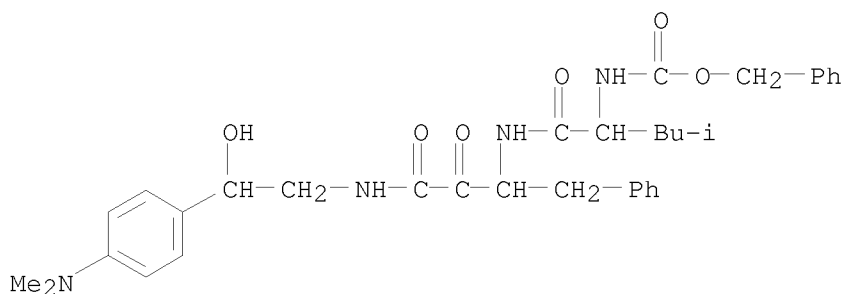
RN 153370-55-9 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-hydroxy-2-(2-naphthalenyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)



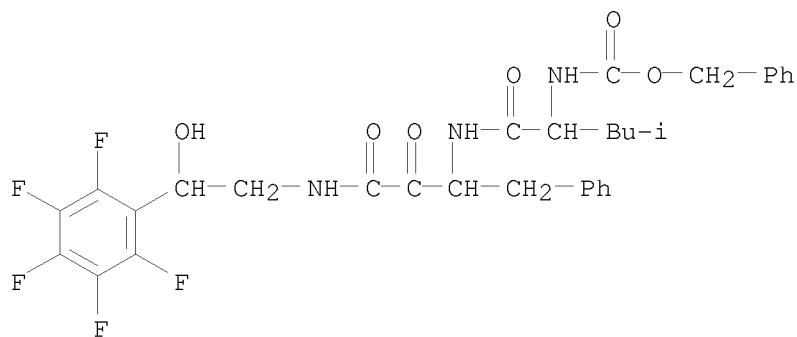
RN 153370-56-0 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[4-(dimethylamino)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



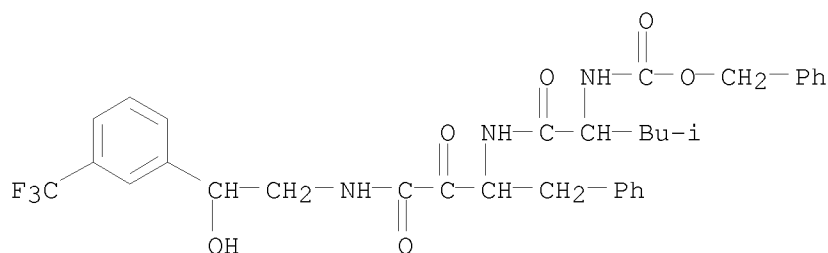
RN 153370-57-1 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(pentafluorophenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



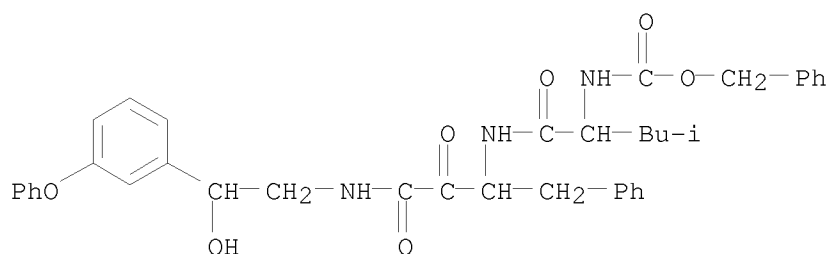
RN 153370-58-2 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



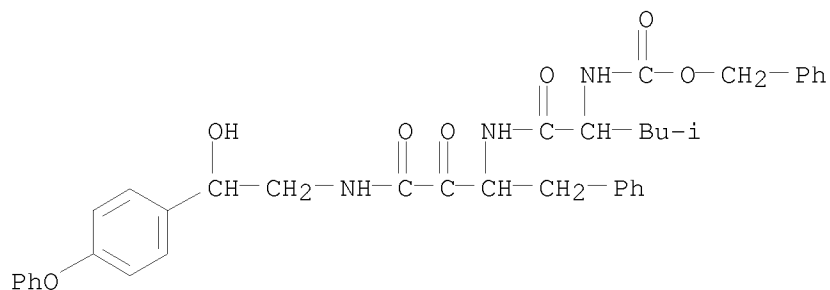
RN 153370-59-3 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(3-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



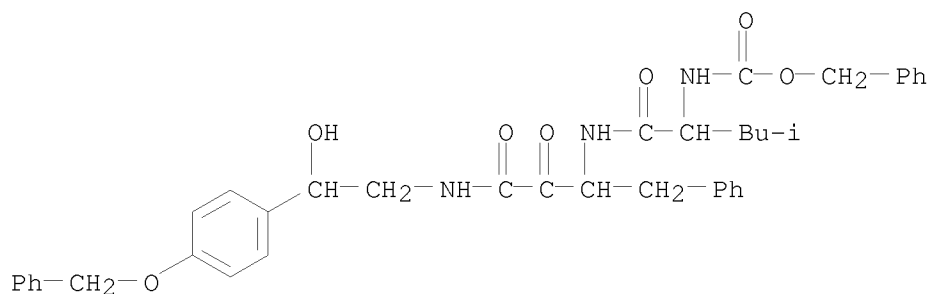
RN 153370-60-6 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-(4-phenoxyphenyl)ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



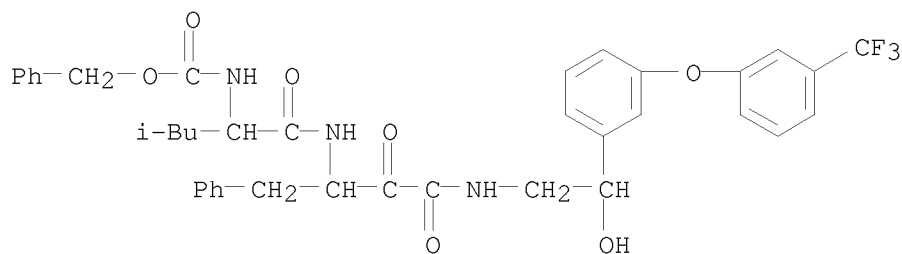
RN 153370-61-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[4-(phenylmethoxy)phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



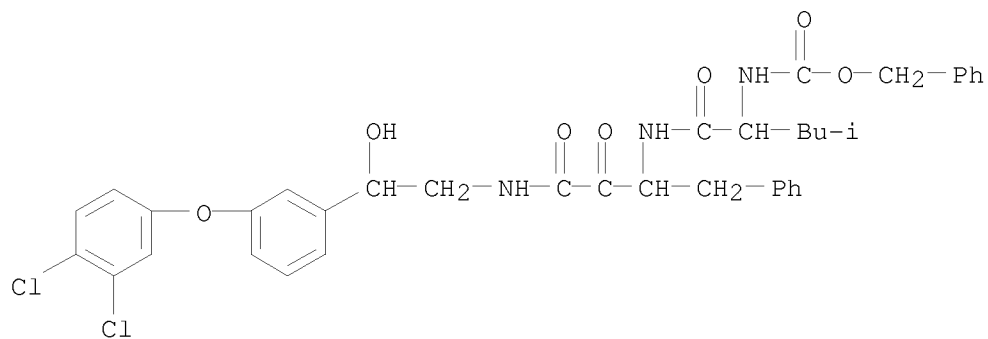
RN 153370-62-8 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-hydroxy-2-[3-[3-(trifluoromethyl)phenoxy]phenyl]ethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



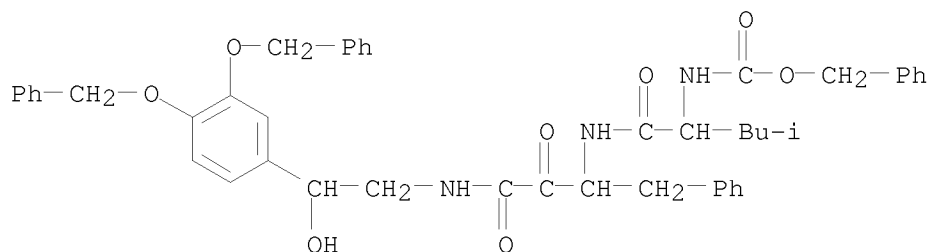
RN 153370-63-9 CAPLUS

CN Carbamic acid, [1-[[[3-[[2-[3-(3,4-dichlorophenoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-64-0 CAPLUS

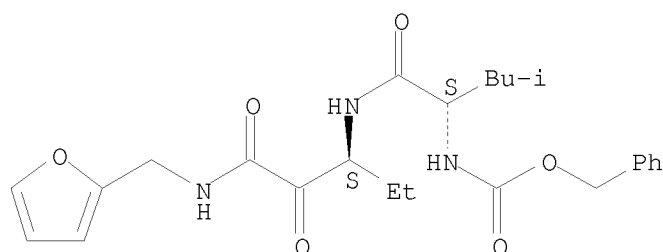
CN Carbamic acid, [1-[[[3-[[2-[3,4-bis(phenylmethoxy)phenyl]-2-hydroxyethyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-65-1 CAPLUS

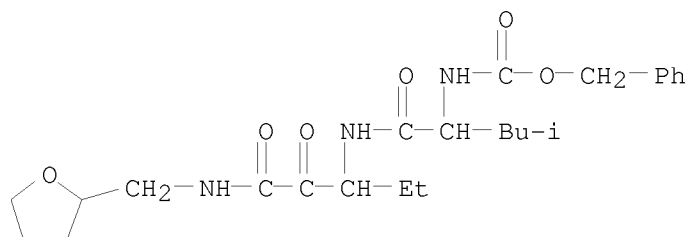
CN Carbamic acid, [1-[[[1-ethyl-3-[(2-furanylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-66-2 CAPLUS

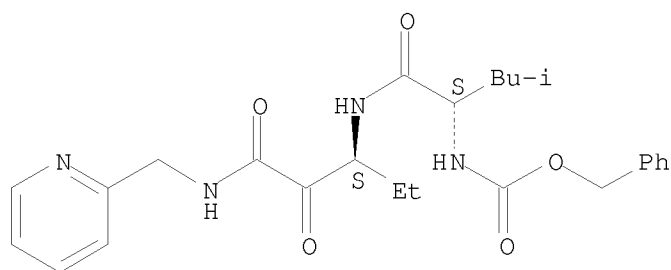
CN Carbamic acid, [1-[[[1-ethyl-3-[(tetrahydro-2-furanyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-67-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

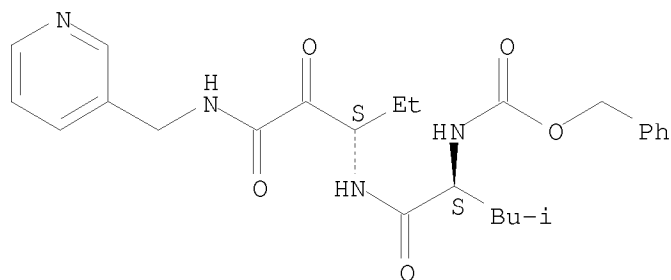
Absolute stereochemistry.



RN 153370-68-4 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(3-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

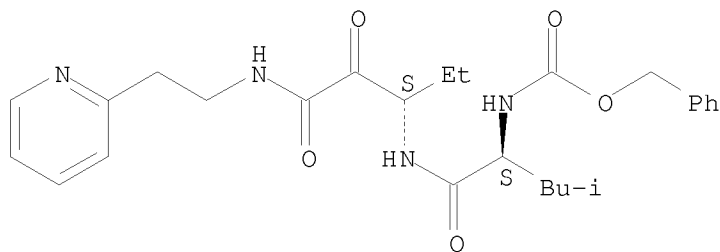
Absolute stereochemistry.



RN 153370-69-5 CAPLUS

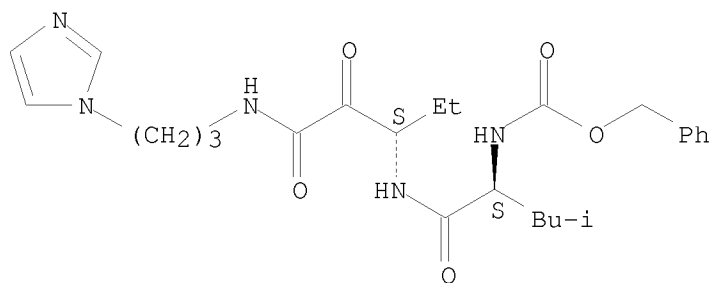
CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[2-(2-pyridinyl)ethyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



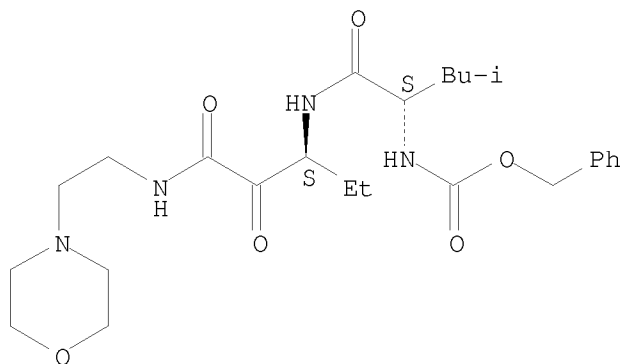
RN 153370-70-8 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[3-(1H-imidazol-1-yl)propyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



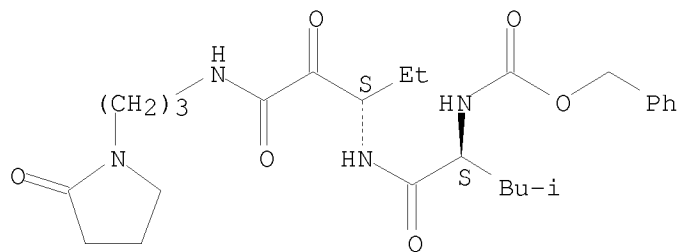
RN 153370-71-9 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(4-morpholinyl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-72-0 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

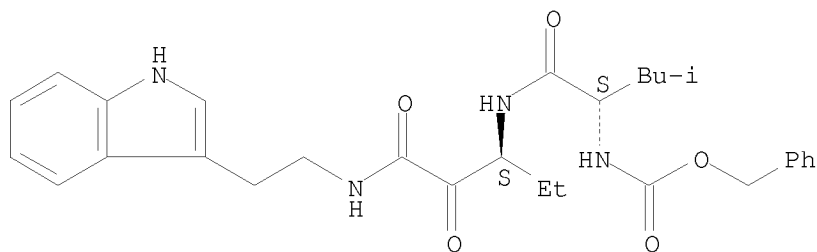
Absolute stereochemistry.



RN 153370-73-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[2-(1H-indol-3-yl)ethyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

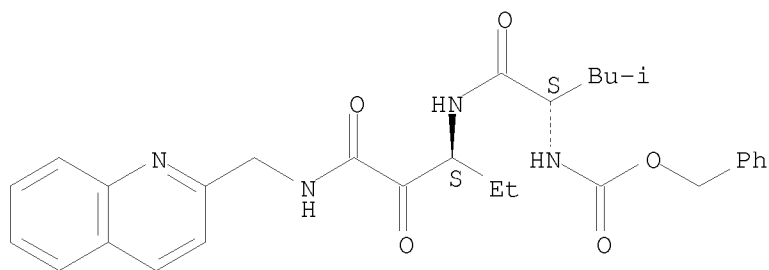
Absolute stereochemistry.



RN 153370-74-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

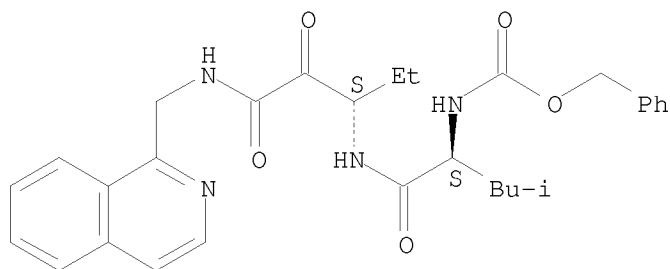
Absolute stereochemistry.



RN 153370-75-3 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[(1-isoquinolinylmethyl)amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

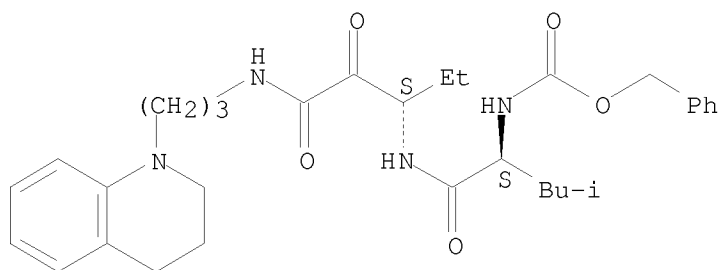
Absolute stereochemistry.



RN 153370-76-4 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

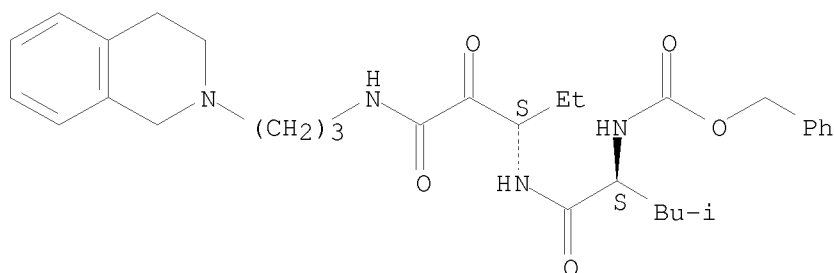
Absolute stereochemistry.



RN 153370-77-5 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-1-ethyl-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

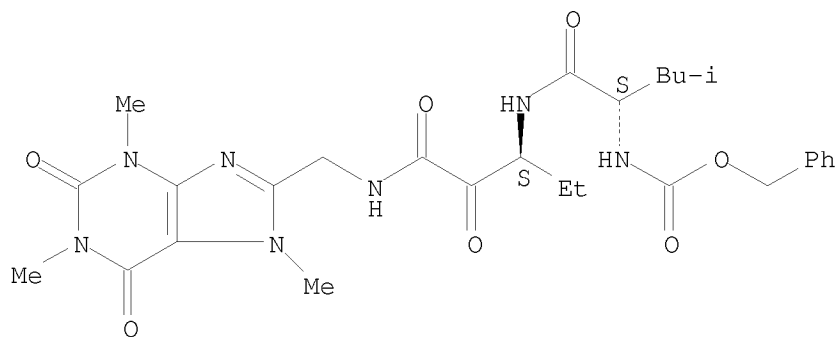


RN 153370-78-6 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[[[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

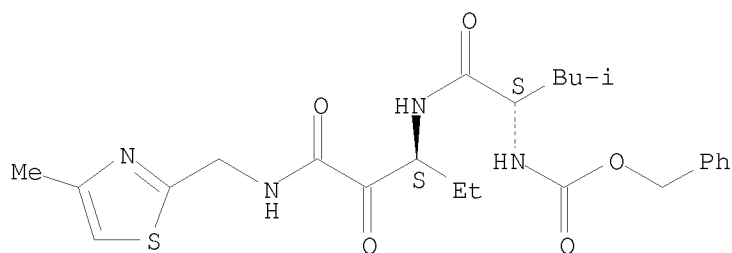




RN 153370-79-7 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[[4-methyl-2-thiazolyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

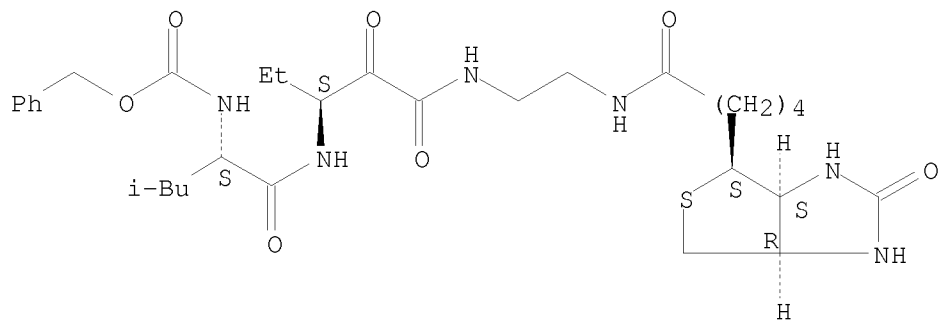
Absolute stereochemistry.



RN 153370-80-0 CAPLUS

CN 2,5,9,12-Tetraazaheptadecanoic acid, 6-ethyl-17-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-3-(2-methylpropyl)-4,7,8,13-tetraoxo-, phenylmethyl ester, [3aS-[3aα,4β(3R\*,6R\*),6aα]]- (9CI) (CA INDEX NAME)

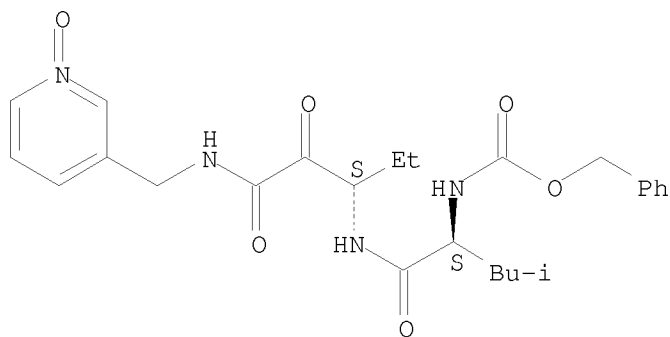
Absolute stereochemistry.



RN 153370-81-1 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-[[[1-oxido-3-pyridinyl)methyl]amino]-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

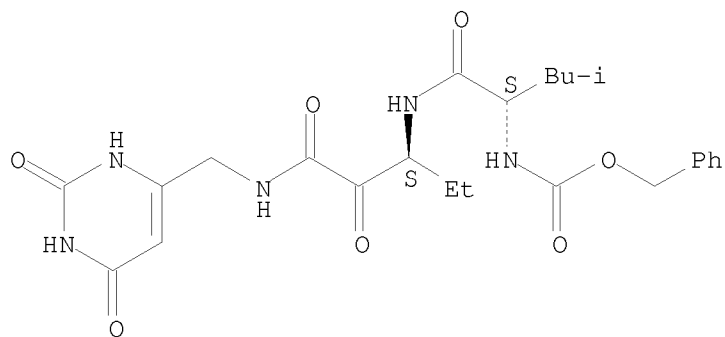
Absolute stereochemistry.



RN 153370-82-2 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-2,3-dioxo-3-[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)methyl]amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

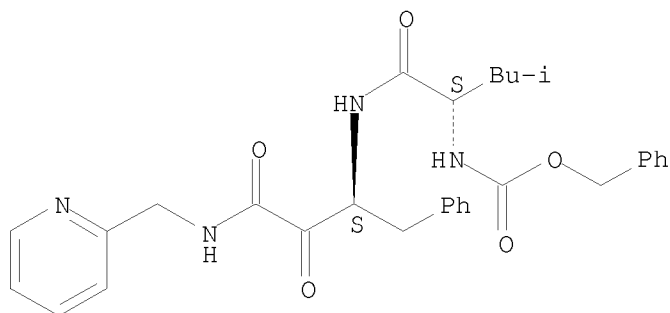
Absolute stereochemistry.



RN 153370-83-3 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-pyridinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

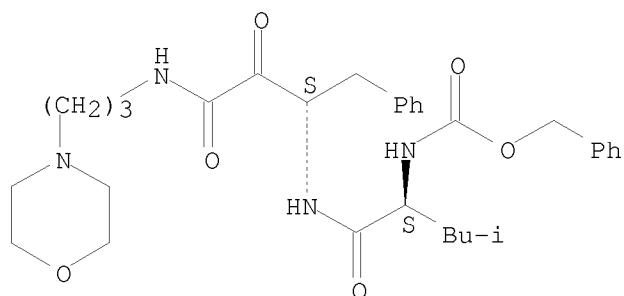
Absolute stereochemistry.



RN 153370-84-4 CAPLUS

CN Carbamic acid, [3-methyl-1-[[[3-[[3-(4-morpholinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]butyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

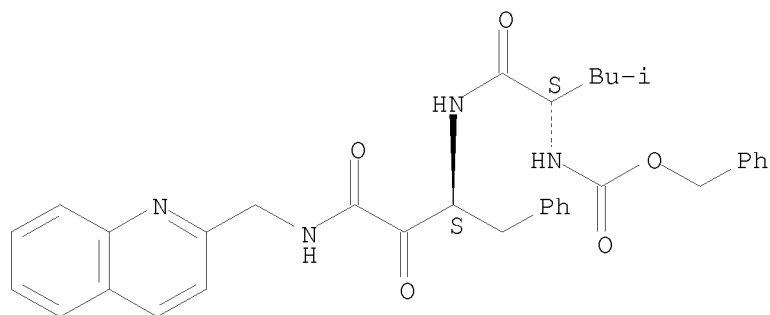
Absolute stereochemistry.



RN 153370-85-5 CAPLUS

CN Carbamic acid, [1-[[[2,3-dioxo-1-(phenylmethyl)-3-[(2-quinolinylmethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

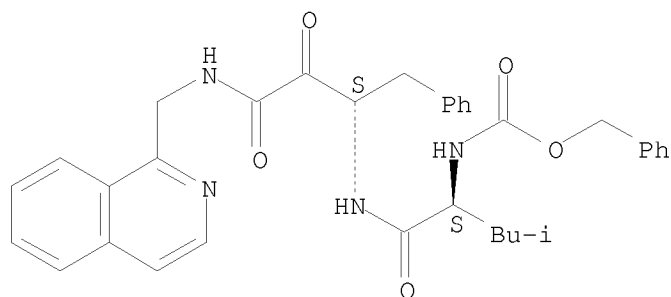
Absolute stereochemistry.



RN 153370-86-6 CAPLUS

CN Carbamic acid, [1-[[[3-[(1-isoquinolinylmethyl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

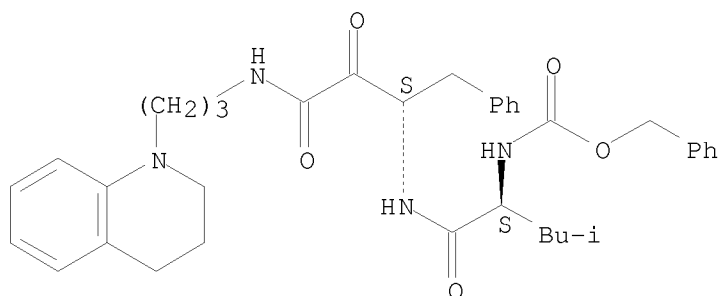
Absolute stereochemistry.



RN 153370-87-7 CAPLUS

CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-1(2H)-quinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

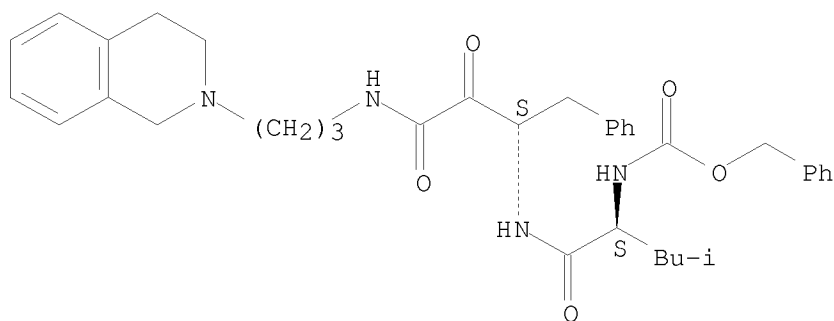
Absolute stereochemistry.



RN 153370-88-8 CAPLUS

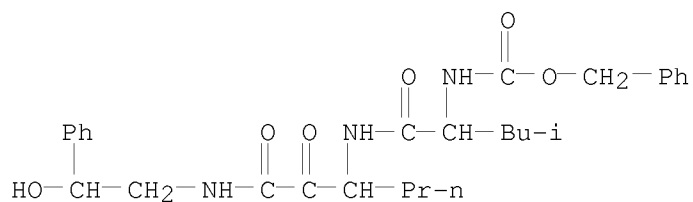
CN Carbamic acid, [1-[[[3-[[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153370-89-9 CAPLUS

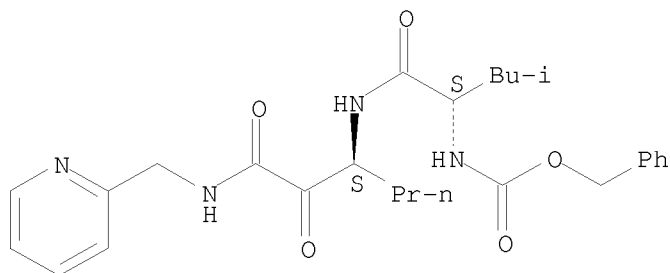
CN Carbamic acid, [1-[[[1-[[[(2-hydroxy-2-phenylethyl)amino]oxoacetyl]butyl]amino]carbonyl]-3-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 153370-90-2 CAPLUS

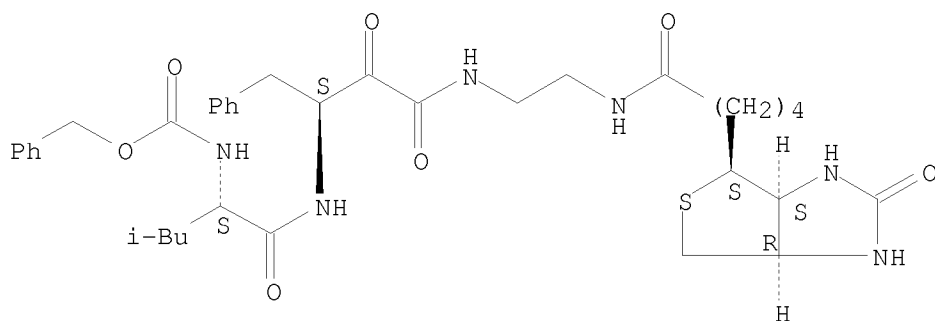
CN Carbamic acid, [3-methyl-1-[[[1-[oxo[(2-pyridinylmethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



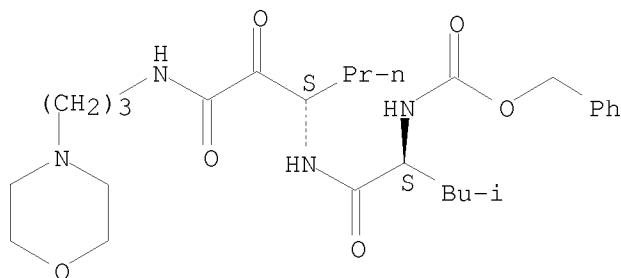
RN 153370-91-3 CAPLUS  
 CN 2,5,9,12-Tetraazaheptadecanoic acid,  
 17-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-3-(2-methylpropyl)-  
 4,7,8,13-tetraoxo-6-(phenylmethyl)-, phenylmethyl ester,  
 [3aS-[3αα,4β(3R\*,6R\*),6αα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



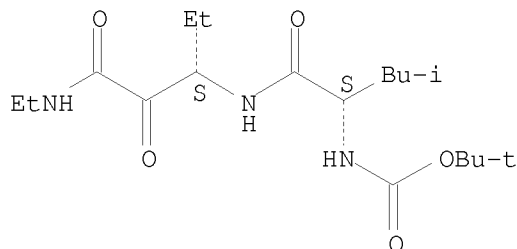
RN 153370-92-4 CAPLUS  
 CN Carbamic acid, [3-methyl-1-[[[1-[[[3-(4-morpholinyl)propyl]amino]oxoacetyl]butyl]amino]carbonyl]butyl]-,  
 phenylmethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153371-08-5 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester,  
 [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> fil stng

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

27.73

504.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-4.00

-35.20

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Nov 21, 2008 (20081121/UP).

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.06

504.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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FILE 'CAPLUS' ENTERED AT 16:00:19 ON 03 DEC 2008

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FILE COVERS 1907 - 3 Dec 2008 VOL 149 ISS 23

FILE LAST UPDATED: 2 Dec 2008 (20081202/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply.

They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d his

(FILE 'HOME' ENTERED AT 15:40:27 ON 03 DEC 2008)

FILE 'REGISTRY' ENTERED AT 15:40:32 ON 03 DEC 2008

L1 STRUCTURE UPLOADED

L2 14 S L1 SAM

L3 291 S L1 FULL

FILE 'CAPLUS' ENTERED AT 15:40:57 ON 03 DEC 2008

L4 51 S L3

L5 1 S US 20070004643 A1/PN

L6 27 S L4 NOT PATENT/DT

L7 17 S L6 AND PD<20041208

L8 24 S L4 NOT L6

L9 22 S L8 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)

L10 39 S L7 OR L9

FILE 'STNGUIDE' ENTERED AT 15:46:12 ON 03 DEC 2008

FILE 'REGISTRY' ENTERED AT 15:58:24 ON 03 DEC 2008

L11 STRUCTURE UPLOADED

L12 14 S L11 SAM SUB=L3

L13 261 S L11 FULL SUB=L3

L14 30 S L3 NOT L13

FILE 'CAPLUS' ENTERED AT 15:59:10 ON 03 DEC 2008

L15 13 S L14

L16 5 S L10 AND L15

FILE 'STNGUIDE' ENTERED AT 15:59:47 ON 03 DEC 2008

FILE 'CAPLUS' ENTERED AT 16:00:19 ON 03 DEC 2008

=> s l15 and (PD<20041208 OR AD<20041208 OR PRD<20041208)

L17 5 L15 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)

=> d ibib abs hitstr 1-5

L17 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:540563 CAPLUS

DOCUMENT NUMBER: 143:60256

TITLE: Preparation of leucyl  $\alpha$ -ketoamide derivatives as calpain inhibitors

INVENTOR(S): Shirasaki, Yoshihisa; Miyashita, Hiroyuki; Nakamura, Masayuki; Inoue, Jun

PATENT ASSIGNEE(S): Senju Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

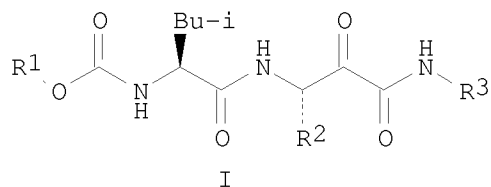
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2006076989 A 20060323 JP 2004-354908 20041208 <--  
 EP 1692098 A1 20060823 EP 2004-807051 20041208 <--  
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 IN 2006KN01379 A 20070504 IN 2006-KN1379 20060523 <--  
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 PRIORITY APPLN. INFO.: JP 2003-415764 A 20031212 <--  
 JP 2004-234164 A 20040811 <--  
 WO 2004-JP18692 W 20041208

OTHER SOURCE(S): CASREACT 143:60256; MARPAT 143:60256  
 GI



AB The invention provides compds. I (R1 is alkyl, alkoxy- or heterocyclylalkyl or heterocyclyl; R2 is alkyl or phenylalkyl; R3 is H, alkyl, halo-, alkoxy- or phenylalkyl or fused polycyclyl), which have potent calpain inhibitory activity, are well absorbed orally and produce good drug levels in blood. Thus, I (R1 = MeOCH2CH2, R2 = PhCH2, R3 = Et) was prepared via peptide coupling reaction and shown to strongly inhibit  $\mu$ -calpain and m-calpain (IC50 = 0.17 and 0.11 uM, resp.).

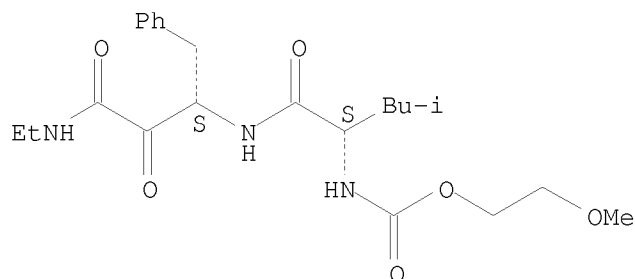
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 854402-70-3P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of leucyl  $\alpha$ -ketoamide derivs. as calpain inhibitors)

RN 854402-43-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

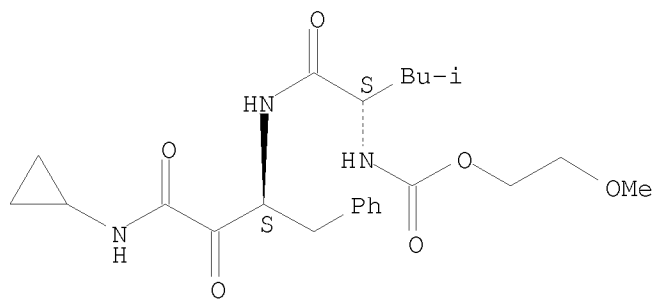




RN 854402-46-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

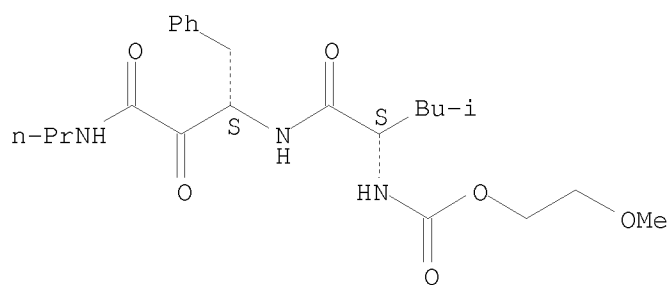
Absolute stereochemistry. Rotation (+).



RN 854402-49-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-(propylamino)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

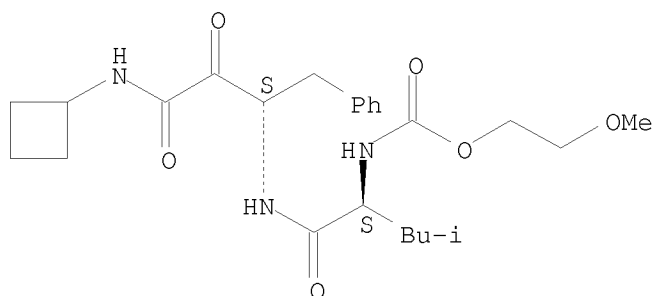
Absolute stereochemistry.



RN 854402-50-9 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclobutylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

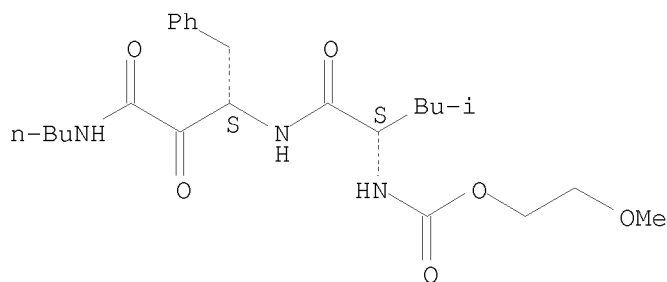
Absolute stereochemistry.



RN 854402-51-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(butylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

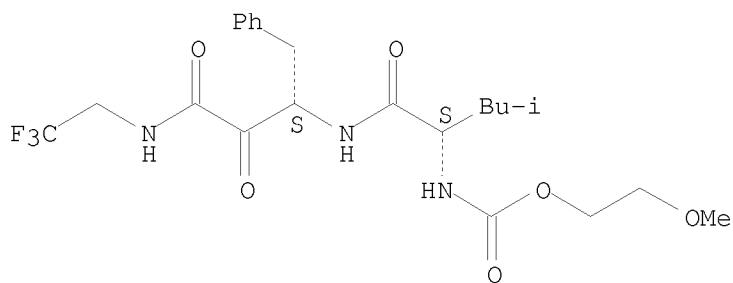
Absolute stereochemistry.



RN 854402-52-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-2,3-dioxo-1-(phenylmethyl)-3-[(2,2,2-trifluoroethyl)amino]propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

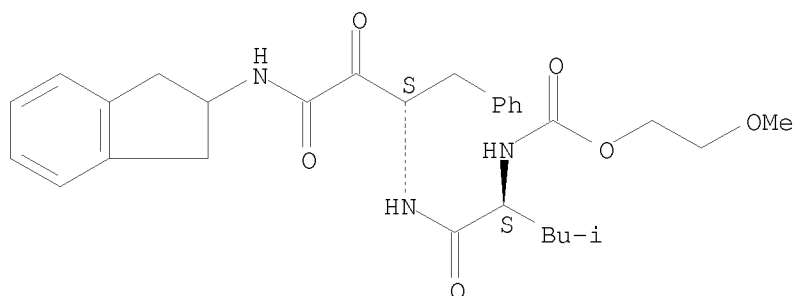
Absolute stereochemistry.



RN 854402-53-2 CAPLUS

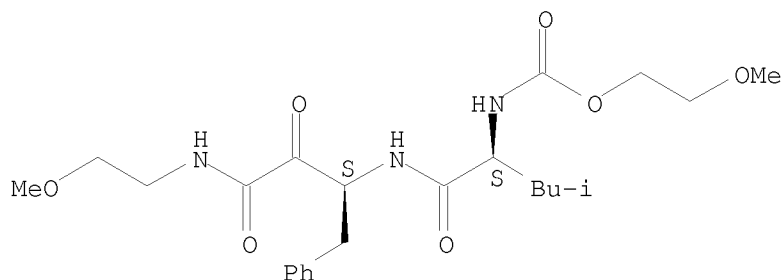
CN Carbamic acid, [(1S)-1-[[[(1S)-3-[(2,3-dihydro-1H-inden-2-yl)amino]-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



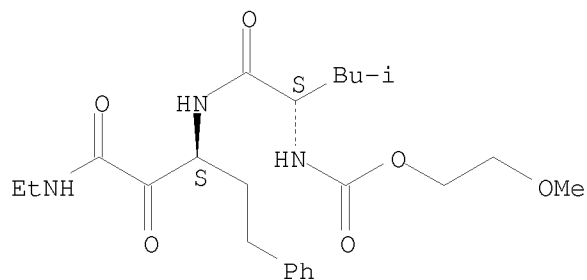
RN 854402-54-3 CAPLUS  
 CN 12-Oxa-2,5,9-triazatridecanoic acid,  
 3-(2-methylpropyl)-4,7,8-trioxo-6-(phenylmethyl)-, 2-methoxyethyl ester,  
 (3S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



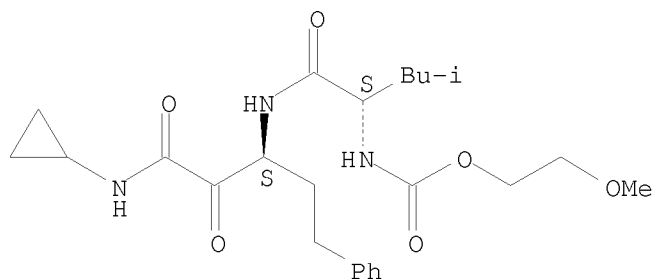
RN 854402-55-4 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(ethylamino)-2,3-dioxo-1-(2-phenylethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 854402-57-6 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(2-phenylethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-methoxyethyl ester  
 (9CI) (CA INDEX NAME)

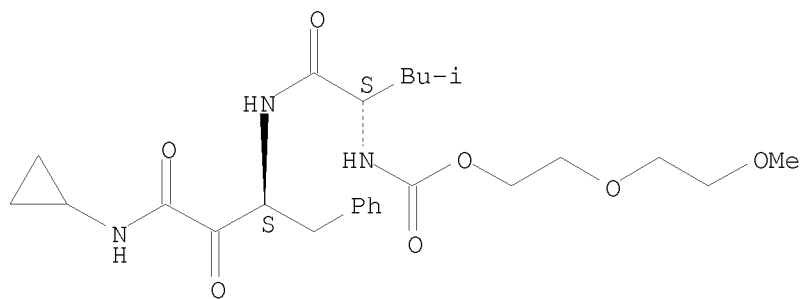
Absolute stereochemistry.



RN 854402-59-8 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-methoxyethoxy)ethyl ester (CA INDEX NAME)

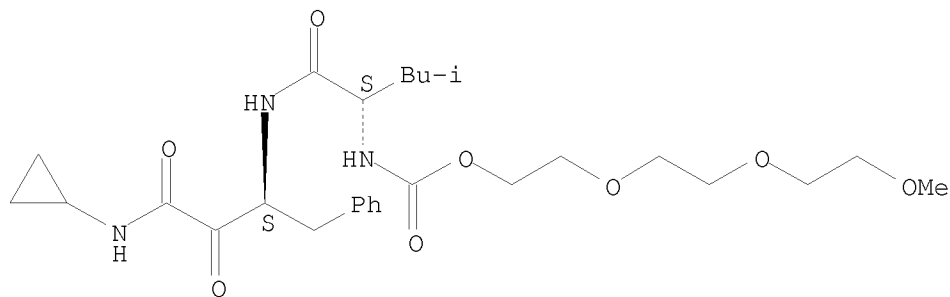
Absolute stereochemistry. Rotation (+).



RN 854402-60-1 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

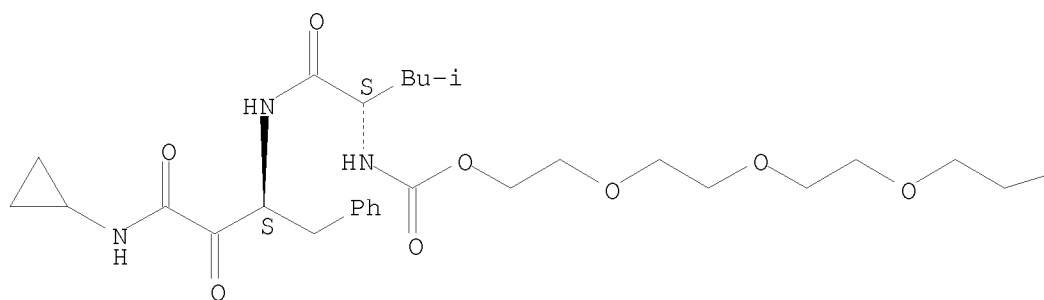


RN 854402-61-2 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 3,6,9,12-tetraoxatridec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



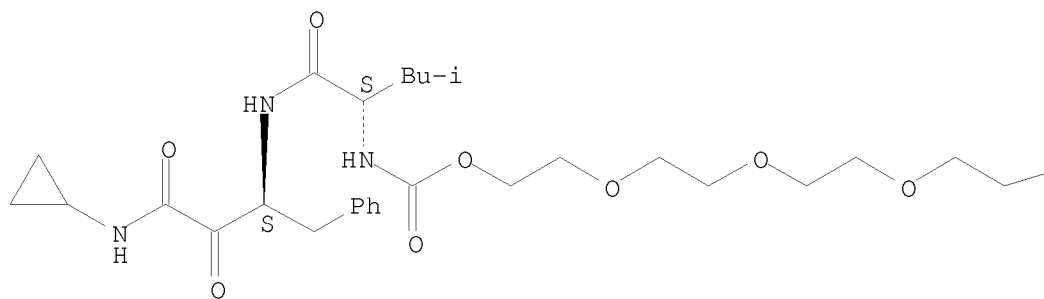
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OMe

RN 854402-62-3 CAPLUS  
CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 3,6,9,12,15-pentaoxaheptadec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

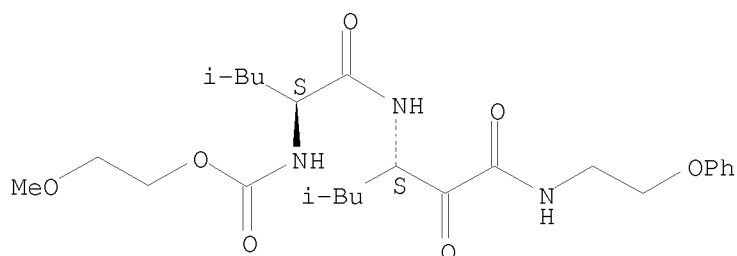


PAGE 1-B

OMe

RN 854402-63-4 CAPLUS  
CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-methyl-1-[oxo[(2-phenoxyethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

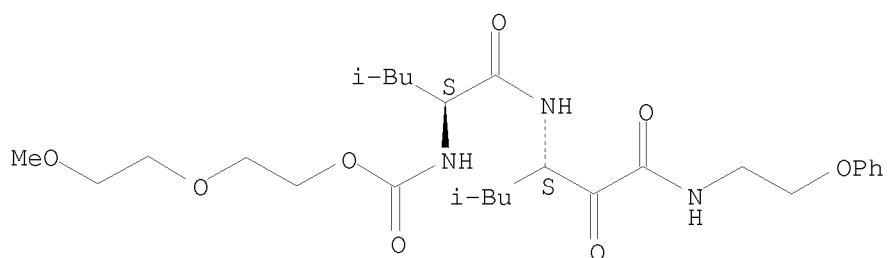
Absolute stereochemistry.



RN 854402-64-5 CAPLUS

CN Carbamic acid, [(1S)-3-methyl-1-[[[(1S)-3-methyl-1-[oxo[(2-phenoxyethyl)amino]acetyl]butyl]amino]carbonyl]butyl]-, 2-(2-methoxyethoxy)ethyl ester (9CI) (CA INDEX NAME)

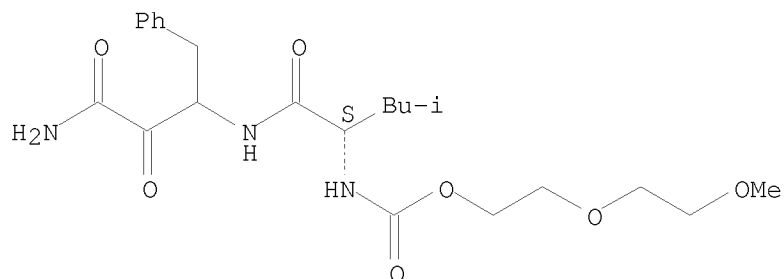
Absolute stereochemistry.



RN 854402-65-6 CAPLUS

CN Carbamic acid, [(1S)-1-[[[3-amino-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-methoxyethoxy)ethyl ester (9CI) (CA INDEX NAME)

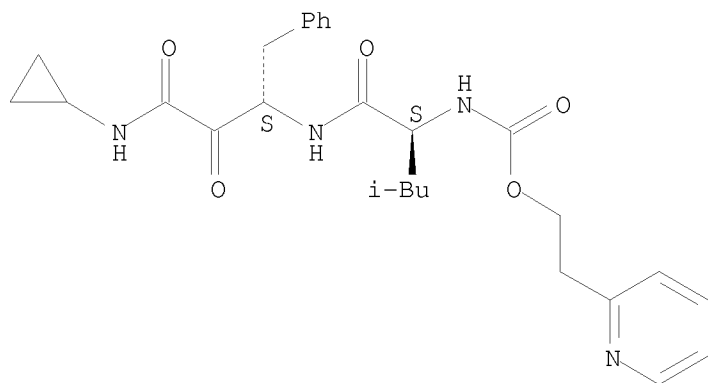
Absolute stereochemistry.



RN 854402-66-7 CAPLUS

CN Carbamic acid, N-[(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(2-pyridinyl)ethyl ester (CA INDEX NAME)

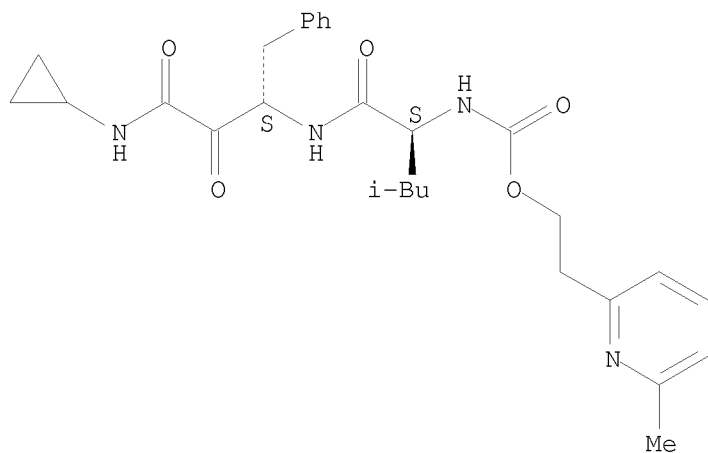
Absolute stereochemistry. Rotation (-).



RN 854402-67-8 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(6-methyl-2-pyridinyl)ethyl ester (9CI) (CA INDEX NAME)

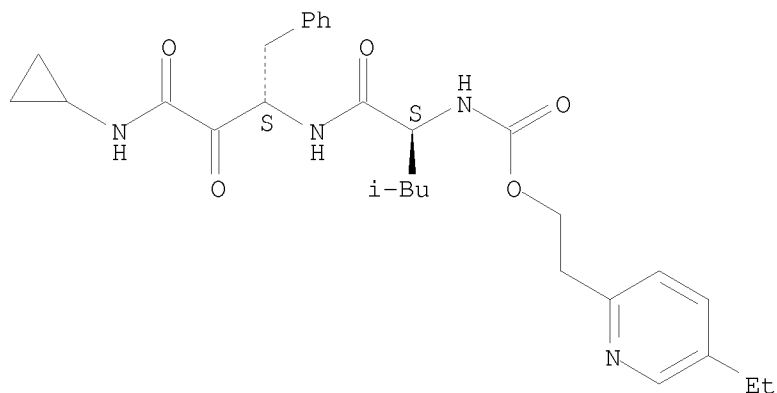
Absolute stereochemistry. Rotation (-).



RN 854402-68-9 CAPLUS

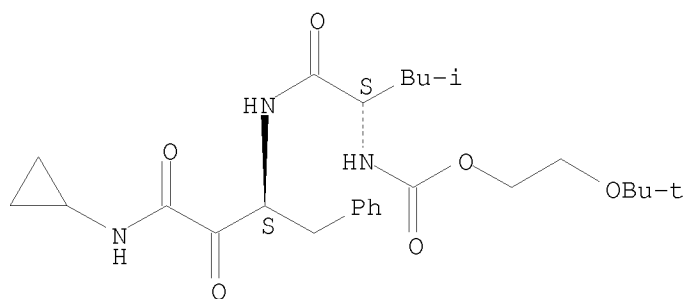
CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(5-ethyl-2-pyridinyl)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



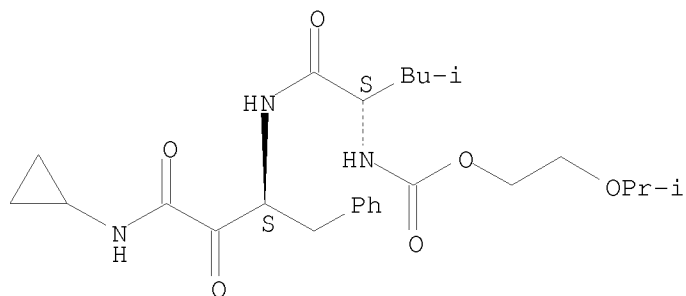
RN 854402-69-0 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(1,1-dimethylethoxy)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 854402-70-3 CAPLUS  
 CN Carbamic acid, [(1S)-1-[[[(1S)-3-(cyclopropylamino)-2,3-dioxo-1-(phenylmethyl)propyl]amino]carbonyl]-3-methylbutyl]-, 2-(1-methylethoxy)ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:875240 CAPLUS



DOCUMENT NUMBER: 139:364944  
 TITLE: Preparation of diketohydrazine derivatives as cysteine protease inhibitors  
 INVENTOR(S): Hatayama, Akira; Tsuruta, Hiroshi; Ochi, Yasuo; Imawaka, Haruo  
 PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 231 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091202	A1	20031106	WO 2003-JP5252	20030424 <--
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PRIORITY APPLN. INFO.:			JP 2002-123796	A 20020425 <--
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			WO 2003-JP5252	W 20030424 <--

OTHER SOURCE(S): MARPAT 139:364944

AB Diketohydrazine (3-amino-2-oxopropanoylhydrazine or 3-aminopropionohydrazide) derivs. represented by the following general formula R-AA1-AA2-NR9CR7R8COCONR10NRYRX [wherein R = H, CycA, halo, (un)substituted C1-8 alkyl, R16CO, R16C(S), R16O2C, R16R17NCO, R16SO2, R16COCH2, R16C(S)CH2; CycA = C3-15 mono-, bi-, or tricyclic carbocyclic ring, 3- to 15-membered mono-, bi-, or tricyclic heterocyclic ring containing 1-4 N, 1 or 2 O and/or 1 or 2 S atom(s); R16 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, CycA; R17, R9 = H, C1-4 alkyl, CycA, CycA-C1-4 alkyl; AA1 = a single bond, (un)substituted NR3CR1R2CO, etc.; R1, R2 = H, (un)substituted C1-8 alkyl, CysA, etc.; R3, R7, R8 = H, C1-8 alkyl, CycA, CycA-C1-8 alkyl, etc.; AA2 = a single bond, NR3CR1R2CO, -CycC-CO-, -NR38-CycD-CO-, etc.; CycC = 3- to 17-membered mono or bicyclic heterocyclic ring; CycD = C3-14 mono or bicyclic carbocyclic ring, 3- to 14-membered mono- or bicyclic heterocyclic ring; R38 = group listed in R17; R10, RY, and RX are not defined] and pharmaceutically acceptable salts thereof are prepared These compds. are inhibitors of cysteine protease, in particular cathepsin K, S, L, B, H, F, Y, or C, calpain, or

caspase 1. Because of having a cysteine protease inhibitory activity, they are useful as remedies for inflammatory diseases, immune diseases, ischemic diseases, respiratory diseases, circulatory diseases, blood diseases, nerve diseases, liver/biliary duct diseases, bone/joint diseases, metabolic diseases, or diseases caused by apoptosis or degradation of bioconstituent proteins. The bone/joint diseases include osteoporosis, chronic articular rheumatism, arthritis, osteoarthritis (arthrosis deformans), hypercalcemia, bone metastasis of carcinoma, or bone fracture. Also disclosed is a bone absorption inhibitor containing the above compound. Because of having an elastase inhibitory activity, these compds. are also useful as remedies for COPD (chronic obstructive pulmonary disease) and so on. N'-(3-tert-butyl-1,3-thiazolidin-2-ylidene)-3-cyclohexylcarbonylamino-2-oxo-3-(tetrahydropyran-4-yl)propionohydrazide hydrochloride inhibited cathepsin K with  $K_i$  of 2.5 nM. A tablet and an ampule containing N'-(3-methyl-1,3-thiazolidin-2-ylidene)-(3S)-3-cyclohexylcarbonylamino-2-oxo-5-methylhexanohydrazide hydrochloride were described.

IT 620612-98-8P 620613-01-6P 620613-02-7P  
620614-12-2P 620614-16-6P 620614-17-7P  
620614-19-9P

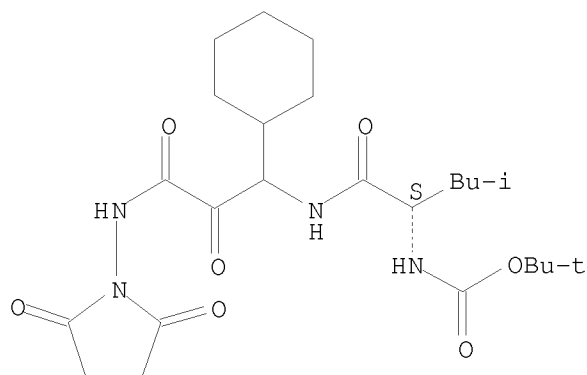
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diketohydrazine derivs. as cysteine protease inhibitors and therapeutic agents)

RN 620612-98-8 CAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-3-cyclohexyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo- (9CI) (CA INDEX NAME)

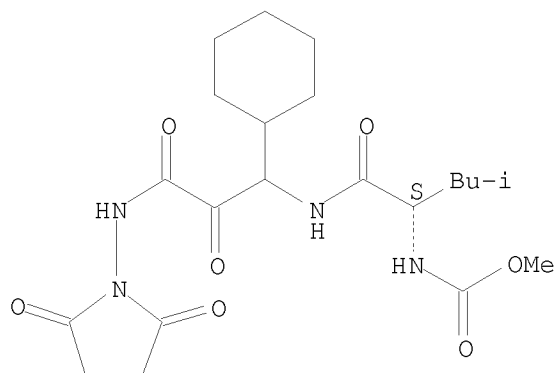
Absolute stereochemistry.



RN 620613-01-6 CAPLUS

CN  $\beta$ -Alaninamide, N-(methoxycarbonyl)-L-leucyl-3-cyclohexyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo- (9CI) (CA INDEX NAME)

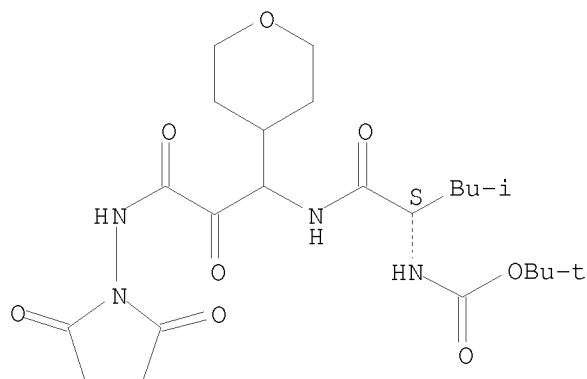
Absolute stereochemistry.



RN 620613-02-7 CAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-N-(2,5-dioxo-1-pyrrolidinyl)-2-oxo-3-(tetrahydro-2H-pyran-4-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

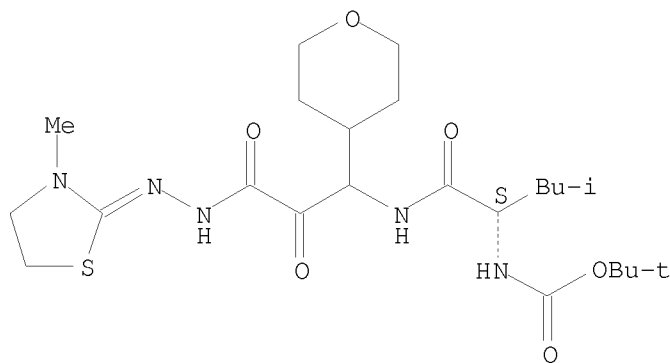


RN 620614-12-2 CAPLUS

CN 2H-Pyran-4-propanoic acid,  $\beta$ -[[[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]tetrahydro- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

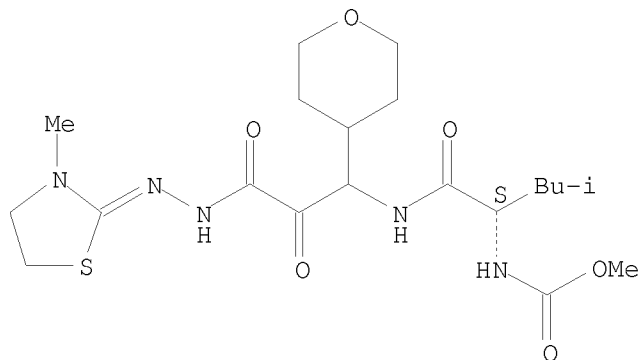


RN 620614-16-6 CAPLUS

CN 2H-Pyran-4-propanoic acid, tetrahydro- $\beta$ -[[[(2S)-2-

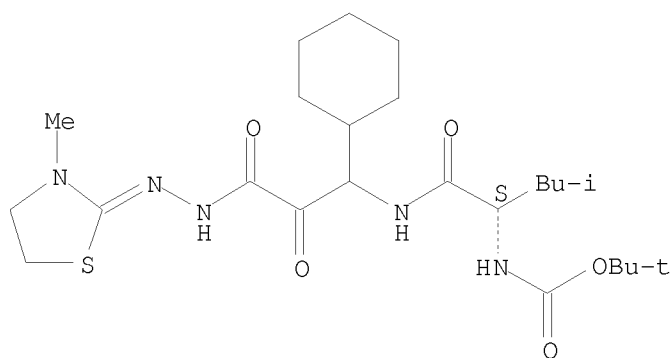
[(methoxycarbonyl)amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-,  
2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



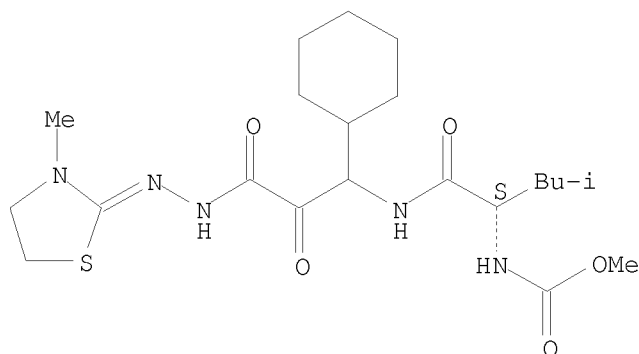
RN 620614-17-7 CAPLUS  
CN Cyclohexanepropanoic acid,  $\beta$ -[[[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



RN 620614-19-9 CAPLUS  
CN Cyclohexanepropanoic acid,  $\beta$ -[[[(2S)-2-[(methoxycarbonyl)amino]-4-methyl-1-oxopentyl]amino]- $\alpha$ -oxo-, 2-(3-methyl-2-thiazolidinylidene)hydrazide (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1995:731521 CAPLUS

DOCUMENT NUMBER: 123:144653

ORIGINAL REFERENCE NO.: 123:25801a,25804a

TITLE: Preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors.

INVENTOR(S): Harbeson, Scott L.; Straub, Julie Ann

PATENT ASSIGNEE(S): Alkermes, Inc., USA

SOURCE: PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

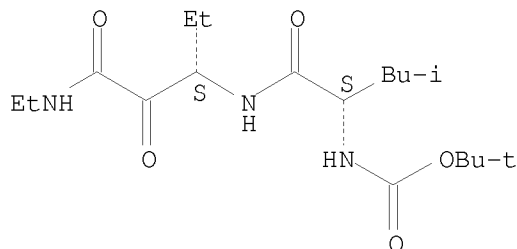
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500535	A1	19950105	WO 1994-US6497	19940609 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5541290	A	19960730	US 1993-82274	19930624 <--
AU 9472452	A	19950117	AU 1994-72452	19940609 <--
PRIORITY APPLN. INFO.:			US 1993-82274	A 19930624 <--
			WO 1994-US6497	W 19940609 <--

OTHER SOURCE(S): CASREACT 123:144653; MARPAT 123:144653

AB M(A1)x<sub>2</sub>NHCHR1COCONHR2SO<sub>2</sub>R3 (sic), M(A1)x<sub>2</sub>NHCHR1COCONHR5R6, etc.; [M = H, H<sub>2</sub>NCO, H<sub>2</sub>NCS, H<sub>2</sub>NSO<sub>2</sub>, R7CS, R7NHCS, R7CO, R7SO<sub>2</sub>, R7O<sub>2</sub>C, etc.; R7 = 1-adamantyl, (substituted) alkyl, alkyl, Ph, naphthyl, phenylalkyl, phenoxyalkyl, etc.; A1 = D-, L-, or nonchiral amino acid, e.g., Ala, Val, Leu, Ile, Met, Tyr, Asn, Gln,  $\beta$ -Ala, Sar, Orn, O-ethylserine, pipercolinic acid, cyclohexylalanine, pyridylalanine, p-nitrophenylalanine,  $\alpha$ -aminoheptanoic acid, citrulline, 2-azetidinecarboxylic acid, trifluoroleucine, etc.; x = 0-3; A2 = D- or L-amino acid capable of imparting calpain specificity; R1 = alkyl, cycloalkyl, fluoroalkyl; R2 = alkyl, cycloalkyl, phenylalkyl, (substituted) phenylalkyl, phenylcycloalkyl; R3 = R2, OH, OR2, NH2, NHR2; NR2R2; R5, R6 = H, alkyl, cycloalkyl, (substituted) phenylalkyl, phenylcycloalkyl, morpholinoalkyl, piperidinoalkyl, etc.], were prepared Thus, Z-Leu-Abu-CONHEt (Abu = L- $\alpha$ -aminobutyric acid) (solution phase preparation given) inhibited calpain I with K<sub>i</sub> = 77 nM.

IT 153371-08-5P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of peptide  $\alpha$ -ketoamides as calpain inhibitors)  
 RN 153371-08-5 CAPLUS  
 CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1995:31017 CAPLUS  
 DOCUMENT NUMBER: 122:133766  
 ORIGINAL REFERENCE NO.: 122:24963a,24966a  
 TITLE: Stereospecific Synthesis of Peptidyl  $\alpha$ -Keto Amides as Inhibitors of Calpain  
 AUTHOR(S): Harbeson, Scott L.; Abelleira, Susan M.; Akiyama, Alan; Barrett, Robert, III; Carroll, Renee M.; Straub, Julie Ann; Tkacz, Jaroslaw N.; Wu, Chichih; Musso, Gary F.  
 CORPORATE SOURCE: Alkermes Inc., Cambridge, MD, 02139-4136, USA  
 SOURCE: Journal of Medicinal Chemistry (1994), 37(18), 2918-29  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Peptidyl  $\alpha$ -keto amides have been synthesized and tested as inhibitors of the cysteine protease calpain. A stereospecific synthesis was devised in which protected dipeptidyl  $\alpha$ -hydroxy amides were oxidized with TEMPO/hypochlorite to the corresponding  $\alpha$ -keto amides. This oxidation was accomplished in good yields and without epimerization of the chiral center adjacent to the ketone. The potent inhibition of porcine calpain I by the L,L diastereomers, combined with the poor inhibition by the L,D diastereomers, established the requirement for the all-L stereochem. of the active inhibitor. The early lead inhibitors were very hydrophobic and, therefore, poorly soluble in aqueous solns. Using the stereospecific route, new compds. were prepared with polar groups at the C- and N-termini. These modifications resulted in more soluble inhibitors that were still potent inhibitors of calpain. Studies of the stability of these  $\alpha$ -keto amides showed that absolute stereochem. can be maintained in acidic and unbuffered environments but general base-catalyzed epimerization of the chiral center adjacent to the ketone occurred rapidly. The  $\alpha$ -hydroxy precursors were inactive as inhibitors of calpain, which supports the hypothesis that the  $\alpha$ -keto compds. reversibly form an enzyme-bound tetrahedral species that results from the nucleophilic addition of the catalytic thiol of calpain to the electrophilic ketone of the inhibitor.  
 IT 153371-08-5P

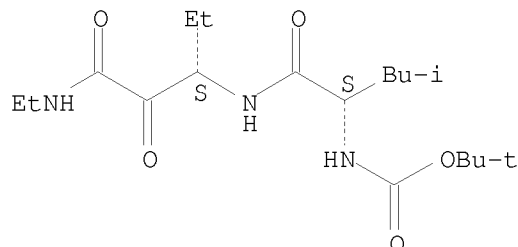
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(stereospecific synthesis of peptidyl  $\alpha$ -keto amides as inhibitors of calpain)

RN 153371-08-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:153723 CAPLUS

DOCUMENT NUMBER: 120:153723

ORIGINAL REFERENCE NO.: 120:26825a,26828a

TITLE: Use of calpain inhibitors in the inhibition and treatment of medical conditions associated with increased calpain activity

INVENTOR(S): Eveleth, David D., Jr.; Lynch, Gary; Powers, James C.; Bartus, Raymond T.

PATENT ASSIGNEE(S): Cortex Pharmaceuticals, Inc., USA; Georgia Tech Research Corp.

SOURCE: PCT Int. Appl., 255 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9400095	A2	19940106	WO 1993-US6143	19930624 <--
WO 9400095	A3	19940317		
W:	AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9345449	A	19940124	AU 1993-45449	19930624 <--
JP 09500087	T	19970107	JP 1993-502621	19930624 <--
PRIORITY APPLN. INFO.:			US 1992-903800	A2 19920624 <--
			US 1993-34996	A2 19930316 <--
			US 1993-72609	A2 19930601 <--
			WO 1993-US6143	A 19930624 <--

AB Medical conditions in mammals (e.g. cardiac muscle tissue damage, cataracts, smooth muscle damage, and vasospasm) associated with increased proteolytic activity of calpain are treated by administering a pharmaceutical composition containing a calpain inhibitor in a pharmacol. effective

amount The inhibitor is a peptide keto compound, substituted heterocyclic compound, or halo ketone peptide. Also, a method of inhibiting proliferation of smooth muscle cells and thereby preventing the restenosis of a blood vessel which has undergone therapeutic angioplasty includes the administration of a calpain inhibitor to the blood vessel during or after the angioplasty. Further, methods of blocking the establishment of the tonically contracted state in smooth muscle and relaxing tonically contracted smooth muscle are disclosed. These methods involve the administration of a calpain inhibitor, thereby reducing or preventing smooth muscle contraction associated with vasospasm and bronchospasm.

IT 153371-08-5

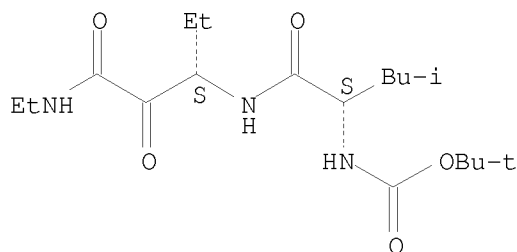
RL: BIOL (Biological study)

(as calpain inhibitor, heart and vascular disease treatment with)

RN 153371-08-5 CAPLUS

CN Carbamic acid, [1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

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FULL ESTIMATED COST

34.57

539.12

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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LAST RELOADED: Nov 21, 2008 (20081121/UP).

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FILE 'REGISTRY' ENTERED AT 15:40:32 ON 03 DEC 2008

L1 STRUCTURE UPLOADED

L2 14 S L1 SAM

L3 291 S L1 FULL

FILE 'CAPLUS' ENTERED AT 15:40:57 ON 03 DEC 2008

L4 51 S L3

L5 1 S US 20070004643 A1/PN

L6 27 S L4 NOT PATENT/DT



L7 17 S L6 AND PD<20041208  
L8 24 S L4 NOT L6  
L9 22 S L8 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)  
L10 39 S L7 OR L9

FILE 'STNGUIDE' ENTERED AT 15:46:12 ON 03 DEC 2008

FILE 'REGISTRY' ENTERED AT 15:58:24 ON 03 DEC 2008

L11 STRUCTURE UPLOADED  
L12 14 S L11 SAM SUB=L3  
L13 261 S L11 FULL SUB=L3  
L14 30 S L3 NOT L13

FILE 'CAPLUS' ENTERED AT 15:59:10 ON 03 DEC 2008

L15 13 S L14  
L16 5 S L10 AND L15

FILE 'STNGUIDE' ENTERED AT 15:59:47 ON 03 DEC 2008

FILE 'CAPLUS' ENTERED AT 16:00:19 ON 03 DEC 2008

L17 5 S L15 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)

FILE 'STNGUIDE' ENTERED AT 16:01:19 ON 03 DEC 2008

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COST IN U.S. DOLLARS

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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

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CA SUBSCRIBER PRICE

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L18 0 L14

=> d his

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FILE 'REGISTRY' ENTERED AT 15:40:32 ON 03 DEC 2008

L1 STRUCTURE UPLOADED  
L2 14 S L1 SAM  
L3 291 S L1 FULL

FILE 'CAPLUS' ENTERED AT 15:40:57 ON 03 DEC 2008

L4 51 S L3  
L5 1 S US 20070004643 A1/PN  
L6 27 S L4 NOT PATENT/DT  
L7 17 S L6 AND PD<20041208  
L8 24 S L4 NOT L6  
L9 22 S L8 AND (PD<20041208 OR AD<20041208 OR PRD<20041208)  
L10 39 S L7 OR L9

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FILE 'REGISTRY' ENTERED AT 15:58:24 ON 03 DEC 2008

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L13           261 S L11 FULL   SUB=L3  
L14           30 S L3 NOT L13

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FILE 'STNGUIDE' ENTERED AT 15:59:47 ON 03 DEC 2008

FILE 'CAPLUS' ENTERED AT 16:00:19 ON 03 DEC 2008

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COST IN U.S. DOLLARS

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FULL ESTIMATED COST

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